User's Guide

Thermo Scientific
HyClone Single-Use Bioreactor

Part of Thermo Fisher Scientific

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Thermo Scientific HyClone Single-Use Bioreactor (S.U.B.) User's Guide

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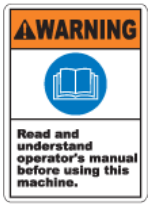
MANUAL NUMBER

REV	ECR/ECN	Date	Description
11	--	10/29/10	S.U.B. User's Guide

Table of Contents

Warnings and Safety



Warning: Read and understand operator's manual before using this equipment.

Thermo Scientific HyClone Single-Use Bioreactor is designed to be operated under traditional mammalian cell culture conditions. A general understanding of bioreactor systems and their operation is important prior to using the system for the first time. ▲

- Read and understand user's manual before operating
- Failure to do so could result in injury

Warning: Hazardous voltage inside

Disconnect power before opening. Service by trained personnel only. Consult manual. Electrical components are designed into and required for the proper function of the Single-Use Bioreactor (S.U.B.) The mixer motor, motor controller, resistive heater jacket and control panel all have electrical components. ▲

- Risk of electrical shock and injury
- There is potential for static charge build-up during mixing and set-up of BPCs

Warning: Entanglement hazard

Rotating parts can cause injury. Keep hands away from moving parts. ▲

Warning: Hot surface. Do not touch.

The heating jacket is designed to heat the outer vessel wall. Normal operating conditions generate heat and could create hot surfaces. ▲

- Hot surface inside
- Contact with surfaces may cause burns
- Do not touch while in operation

Warning: Burst Hazard

Under normal operating conditions the S.U.B. BPC chamber is under slight pressure. Normal passive venting prevents any excess of pressure building up within the chamber. Chamber pressure and inlet line pressure should be monitored for proper settings. ▲

- Contents under pressure
- Do not exceed 0.5 psi (0.03 bar) BPC pressure
- Do not exceed 5 psi (0.34 bar) inlet pressure
- Assure vent filter is properly positioned and working properly

Protective Earthing

Protective earthing must be verified prior to plugging the S.U.B. into any electrical outlet. Ensure the receptacle is properly earth grounded.

Environmental Conditions

- Operating: 17°C to 27°C; 20% to 80% relative humidity, non-condensing
- Storage: -25°C to 65°C
- Installation category II (over voltage) in accordance with IEC 664
- Altitude Limit: 2,000 meters

Water Jacket Vessel Information

The Water Jacket S.U.B. has been designed to be operated with water as the heat transfer medium with temperatures not exceeding 50°C (122°F) under less than 150 psi (1 MPa) operating pressure.

NOTE: The S.U.B. BPC operating limits for temperature are 5 to 40°C. The internal pressure should not exceed 0.5 psi. The water jacket is not classified as a pressure vessel and is not required to be registered, inspected and stamped with the Code U symbol per section U-1(c)2(f) of the ASME Boiler and Pressure Vessel Code [operating with water as the heat transfer medium, temperature not exceeding 99°C (210°F) under less than 300 psi (2 MPa)]. In Europe, all pressure vessels and assemblies operating at pressures greater than 7.5 psi (50 MPa) are subject to the Pressure Equipment Directive 97/23/EC (PED). As required by this directive, a conformity assessment performed by the manufacture deemed this equipment as falling below the conformity assessment category 1 (type of equipment – vessel, state of the intended fluid contents – liquid, fluid group of the intended contents – group 2 [non-dangerous, water]). As such, these vessels are not deemed as being subject to a conformity assessment and are thereby only required to meet the Sound Engineering Practice (SEP) guidelines outlined in the directive. Installation and operation of the S.U.B. must adhere to the manufacturer's operating guidelines in order to ensure compliance with this assessment; to ensure utmost safety it is recommended that all S.U.B jacket systems be operated at 75 psi or less. If regulatory certification is deemed necessary by a governing body or the installation is likely to require function outside of the above mentioned parameters, a regulatory stamped jacket can be obtained for an additional fee.

Section 1 Single-Use Bioreactor (S.U.B.) Overview

This section covers the following information:

1.1 Introduction

The Thermo Scientific HyClone Single-Use Bioreactor (S.U.B.) has been designed to be a disposable alternative to conventional stirred tank bioreactors currently utilized in animal cell culture. Based on years of accepted stirred tank reactor (STR) design, the S.U.B. emulates STR scalability and operating parameters, yet it has the unique advantage of being a completely disposable device. Ease of setup with respect to system operation and integration into existing facilities makes the S.U.B. an attractive alternative to its stainless steel counterpart. Critical design parameters such as height to diameter ratios, mixer design and location, and typical control system interfaces have been maintained. The S.U.B. BPC is supplied sterilized by irradiation and therefore does not require any facility hook-ups for sterilization or cleaning. A key element to the single-use design is the plastic (polyethylene) impeller with a bearing/seal assembly linking to an external mixer drive. Quick setup and change over allows for faster turnover in cell culture runs over traditional reusable systems.

The S.U.B. systems consist of three primary components:

1. **Outer support container** with either Electric Resistive or Water Jacket heating systems
2. **Single-Use Bioreactor BioProcess Container (BPC)** and
3. **Control System** for agitation (Electric Resistive and Water Jacket) and temperature (resistive only)

The **outer support container** is engineered and fabricated to fully support each S.U.B. BPC and allow easy access for operation. It is a stainless steel vessel which holds and supports the BPC. The outer support container contains the mixing drive, silicone heating blanket (Electric Resistive) or Water Jacket, controllers for mixing and heating (Electric Resistive), and

portable dolly. The drive shaft is detachable and reusable and is inserted into the BPC through the mixing assembly and into the bearing port. Load cells are offered standard on the 1000 and 2000 L S.U.B.s and are optional for the smaller volume systems.

The **BPC** includes the impeller assembly, sparger, vent filter inlet/outlet ports, probe integration ports, and filling, dispensing, and sampling ports. Each S.U.B. BPC comes fully assembled and gamma irradiated. The materials are fully qualified for biological product contact per USP Class VI plastics. Each assembly is manufactured under cGMP and is supported by qualification and validation information. No reuse cleaning or sterilization validations are required as the BPC is provided gamma irradiated. Innovative, proprietary technology allows for the integration of the mixing shaft, pH and dissolved oxygen probes, and the resistive temperature detector (RTD). The **probe** and **temperature** interfaces are comparable to traditional systems with the design allowing for simple, aseptic connections. Integrated disposable **spargers** are built into the S.U.B. BPC through universal ports.

The **control system** encompasses both incorporated and end-user supplied components. Controls for temperature (resistive only) and agitation are integrated into the S.U.B., with pH/dissolved oxygen (DO) probes and controls being supplied by the user. Water Jacket systems require a temperature control unit selected and supplied by the end user. This User's Guide covers the setup, operation, maintenance and troubleshooting of all retrofit S.U.B. systems in the following volumes – 50, 100, 250, 500, 1000 and 2000 L.

Figure 1.1. Single-Use Bioreactor

1.2 Hardware Characteristics

System Features

The Single-Use Bioreactor is designed for system mobility and easy disposable integration while utilizing a straightforward operator interface. Hardware drawings and specifications tables specific to volume can be found in Section 3. The following sections describe the hardware components of the S.U.B.

Agitation

Stirring speed is adjusted by using the keypad interface on the control panel. The agitation control interface utilizes a digital display to indicate stirring speed in units of revolution per minute (RPM). Power is supplied to the motor by a two position power switch. The up and down arrows on the agitation keypad adjust the stirring speed.

Bioreactor Control System

The Single-Use Bioreactor is designed to integrate with existing bioreactor control systems in their numerous configurations. The S.U.B. control system manages the selected process parameters of agitation and temperature. Parameters of pH and DO control must be managed by an external controller supplied by the end user.

Exhaust Vent Filter Heater

An optional exhaust vent filter heater is available for increased longevity of the exhaust filter on the S.U.B. BPC. Heating the filter sufficiently to eliminate the formation of condensation is an effective means of reducing the risk of fouling of the filter membrane. The heater is factory preset to operate between 40-50°C, but can easily be adjusted to the demand of the application. Temperature settings above 60°C are not recommended.

Condenser System

The Condenser System is recommended for 2000 L S.U.B. use and is also available as optional hardware for smaller systems. It cools exhaust gases and re-circulates the condensate into the bioreactor.

Temperature

The S.U.B. can be operated within the temperature range from ambient to 40°C. For resistive heater systems, temperature setpoints can be adjusted via the temperature controller located on the front panel of the S.U.B. control box. This controller is preprogrammed to avoid overshoot during heat up and maintain a target temperature of +/-0.5°C based on the set value display. The process temperature is measured by means of a supplied RTD (pt-100) that is inserted into the thermo-well of the S.U.B. BPC. Water Jacket system temperature control is maintained through the temperature control unit (TCU) supplied by the end user.

Heating Performance

Heating times for the S.U.B. systems vary based upon operating liquid volume and temperature, ambient or heating fluid temperature, sparge rate, and mixing rate. Users should adjust process liquid staging and seeding strategies to the unique aspects of the S.U.B. Process controllers and heaters in resistive heating systems are designed to provide optimum heat transfer and to minimize heat up times, while maintaining the material integrity of the polymer film construction of the S.U.B. BPC. Refer to Section 1.8 for expected heating times.

External Control

Users can choose to bypass the temperature and mixing speed control system provided with the S.U.B. and utilize existing bioreactor controllers. Refer to Section 1.8 for more details.

Load Cells

Load cells are standard on the 1000 and 2000 L S.U.B. hardware and optional for the smaller S.U.B. volumes. Load cell kits can be installed at the factory or can be added later by a certified service technician. The load cell kit comes with three load cells, summing block, wiring and display with a choice of several data interfaces.

Load cells arrive uncalibrated; it is recommended that the load cell manufacturer or a qualified technician calibrate these systems on site.

1.3 End User Supplied Components

pH and Dissolved Oxygen (DO) Probes

The following table shows the length and diameter requirements for traditional sensors (probes) that can be integrated into the S.U.B. These requirements are based on the necessary insertion depth of the probe when used with the probe ports. **Note:** The presence of a properly positioned O-ring on the probe is critical for use with the S.U.B.

Recommended pH/DO Probes for use with the S.U.B.					
Probe Lengths (from O-ring to tip) Must Not Exceed 235 mm				O-ring to probe tip	
				Print/Lit.	Actual
Probe	Part Number	Diameter (mm)	Thread Type	Length (mm)	Length (mm)
AppliSens DO	Z010023520	12	13.5 PG	235	235
Applisens pH	Z001023510, Z001023511	12	13.5 PG	235	235
Mettler Toledo DO	InPRO 6800/12/220, PN 52200966	12	13.5 PG	215	215
Mettler Toledo pH	405-DPAS-SC-K8S/225, PN 1040544811G	12	13.5 PG	195	219
Broadley-James DO	D140-B220-PT-D9	12	13.5 PG	215	214
Broadley-James pH	F-635-B225-DH	12	13.5 PG	225	219
Finesse DO	DOS-OFF-VP-225	12	13.5 PG	225	220
Finesse pH	PHS-EFP-K8-225	12	13.5 PG	225	220
NOTE: Consult probe manufacturer's Web site for appropriate probe cable connection and part number. ▲					

Table 1.1. Manufacturers and models of S.U.B. compatible pH/DO probes.

Controllers

Many bioreactor controllers can be adapted for use with the S.U.B. Table 1.2 lists several companies offering control systems or custom solutions that will work well when controlling S.U.B. parameters such as dissolved oxygen (DO) and pH. Alternatively, users seeking advanced control functionality and data logging capabilities for parameters of pH, DO, temperature, agitation and others, can determine their own preferred approach in order to interface these parameters with a single controller. Please refer to the Equipment Turnover Package (ETP) supplied with each hardware system for electrical schematics. Discussions regarding the

integration of specific bioreactor control systems for advanced control functionality should be directed though technical support staff for Thermo Scientific HyClone products and the associated controller manufacturer.

Controller Manufacturer
ABEC
Applikon
Allen-Bradley
Bellco
Broadley-James
Das Gip
Emerson
Finesse
Honeywell
New Brunswick Scientific
PendoTech
Sartorius Stedim Biotech
Siemens
Thermo Systems

Table 1.2. Some Controller Manufacturers of S.U.B. compatible pH/DO controllers.

Note: The S.U.B. will work well with any of the various control system platforms, such as PLC, PC, DCS or proprietary operating system based controllers.

1.4 BioProcess Container Characteristics

Single-Use Bioreactor BPC Features

The cell culture itself is contained inside the Single-Use Bioreactor BPC. The chamber is manufactured from CX5-14 film which is a co-extruded structure specifically designed for biopharmaceutical process usage. All materials are qualified for a broad range of physical, mechanical, biological and chemical compatibility requirements. (Refer to CX5-14 data in our BPC Catalog, contact your sales representative for a copy). The bioreactor BPC is pre-sterilized using validated gamma irradiation processes.

Operating Pressure

The S.U.B. BPC does not operate as a closed system, as it has both inlet and exhaust filters that are utilized to maintain an environment for cells to grow without concern for contamination. However, conditions can be encountered when gas inlet flow rate may exceed exhaust flow rate. This may be encountered in the unlikely event of a pressure regulator failure on a gas feed, or when excessive foaming creates conditions of vent blockage. **The S.U.B. BPC is not rated as a pressure vessel (gas pressure should not exceed 0.5 psi within the BPC).** Custom BPCs can be ordered with an optional disposable pressure transducer for monitoring the pressure within the S.U.B. (supplied standard with 1000 and 2000 L systems).

Working Volume

Each S.U.B. is designed for a working volume range. The minimum working volume and the rated working volume are listed in the specification tables provided in Section 3. The total volume listed includes the headspace needed for proper aeration and gas management. Actual working volumes should not exceed the indicated rated working volumes. In addition, working volumes less than the minimums listed can result in damage to the S.U.B. BPC and hardware malfunction.

Draining and Harvest

The S.U.B. is equipped with a bottom drain line that allows for liquid harvest by means of peristaltic pump. Connection of the bottom drain line can be accomplished by use of a tubing welder or the aseptic connection of quick connect or fitting that is provided. Manipulation of the S.U.B. BPC as the last few liters of media is removed can minimize liquid hold-up within the S.U.B.

Aeration

Gas to liquid mass transfer in cell culture bioreactors is controlled by the solubility of the gas in the liquid, its distribution, and the temperature and pressure. Direct air sparging is a way of providing for the oxygen requirements of mammalian cell cultures. The standard S.U.B. bag incorporates a unique disposable dual sparging design that allows for optimal aeration of the culture process and effective CO_2 stripping.

Aseptic Connections

Multiple aseptic connection options exist for S.U.B. users. The standard BPCs include tubing welder sections, quick connects and Pall Kleenpak connections. The S.U.B. BPC is designed with various lengths and dimensions of thermoplastic tubing for the purpose of addition to and dispensing from the S.U.B. BPC. Refer to Ordering Information in Section 3 for custom end treatment options.

Sampling

The S.U.B. is equipped with a small volume sample port that is adjacent to the S.U.B. BPC thermo-well. This small diameter silicone dip tube of 6” length (15.24 cm) allows low void volume samples to be taken for cell viability and density, as well as analyte analysis. This dip tube is supplied with an aseptic luer lock connector (SmartSite) that allows for direct sampling or attachment of various sampling manifolds by use of standard luer lock connection. Alternatively, manifolds can be welded onto the C-Flex sample line by tubing welder.

BPC drawings and standard configuration tables specific to volume can be found in Section 3.

BPC Features

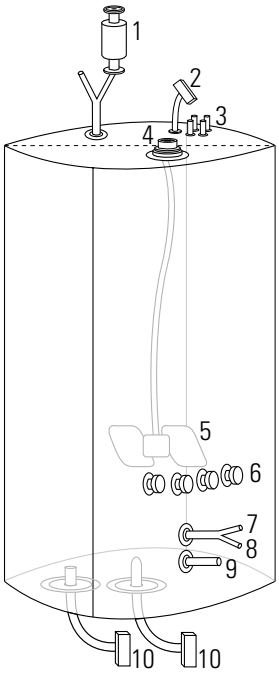


Figure 1.2. Typical 50 L, 100 L and 250 L BPC Schematic

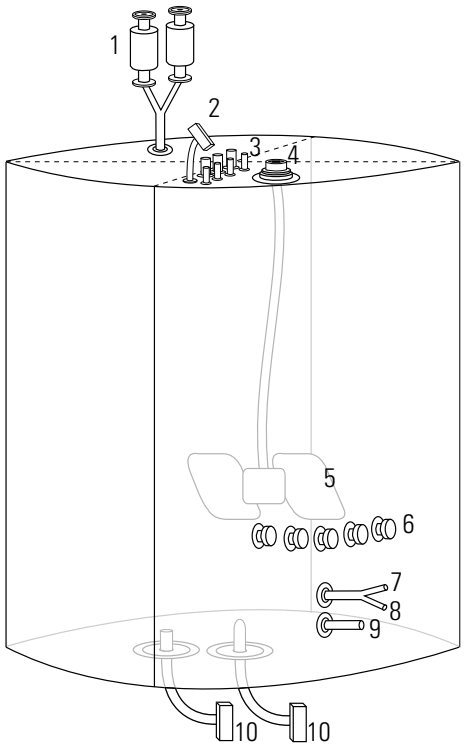


Figure 1.3. Typical 500 L and 1000 L BPC Schematic

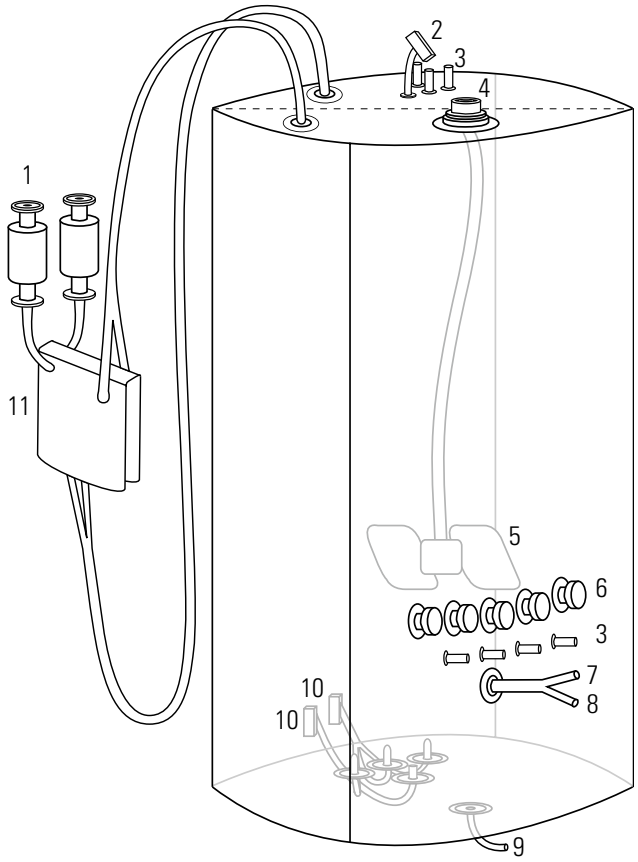


Figure 1.4. Typical 2000 L BPC Schematic

	Part	Description
1.	Exhaust Vent Filter	Single-use capsule filter for exhaust gas exchange
2.	Gas Overlay Port	Protected by gas filter
3.	Ports	For addition of media and other liquids
4.	Seal/Bearing Assembly	Links with mixer motor and allows impeller to turn while retaining integrity of the S.U.B. BPC
5.	Impeller	Injection molded plastic; Linked to seal/bearing assembly by C-Flex tubing contact material of the shaft
6.	Ports with Kleenpak Connectors	For integration of standard 12 mm monitoring pH and DO probes
7.	Temperature RTD Port	For integration of temperature probe while retaining integrity of the S.U.B. BPC
8.	Sampling Port	For needleless sampling or connection to sampling manifold
9.	Drain Port	Used when draining the S.U.B.
10.	Gas Sparge Lines	Sparge integrated into the chamber; Protected by gas filters
11.	Condenser System Bag	Integrates with chill plate to remove condensate from exhaust

Table 1.3 Key to Figures 1.2, 1.3 and 1.4

1.5 Additional System Components

Probe Integration

The probe assembly is an innovative disposable design to package user supplied pH and DO probes for sterilization and to aseptically connect them to the S.U.B. BPC. The probe assembly (Figure 1.5) includes the following components:

1. Molded bellows cover
2. Threaded probe adaptor
3. Pall Kleenpak Connector (KPCHT Series - high temperature)
4. Cable ties

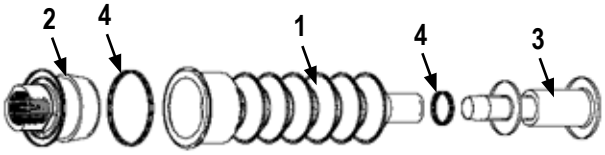


Figure 1.5. Probe Assembly

Required and Optional Accessories

To assist in the operation of the Single-Use Bioreactor the following additional accessories are available (see Section 3 for ordering information):

- Heavy duty tubing clamps - sold separately
  Required (typically four or five)
- Autoclave tray for probe kits (stainless steel)
  Required (minimum of one required) - The autoclave support tray provides an inclined fixture for two probes during autoclaving to minimize stress on the probes and to prevent collapse of the silicone bellows.
- Sampling manifold with luer lock
  Optional
- S.U.B. temperature sample port (for RTD calibration/validation)
  Optional
- Vent Filter Heater System
  Optional - For users who require additional protection for the exhaust vent filter on the standard S.U.B. BPC. Consists of filter heater, programmable controller and power cord.
- Condenser System
  Recommended for 2000 L S.U.B. Optional on smaller systems.
- Load cells
  Standard on 1000 and 2000 L S.U.B.s. Optional on smaller sizes - Consists of three load cells, summing block, wiring and display with choice of several data interfaces.

1.6 Initial Installation Instructions

Hardware Shipment and Setup

The Single-Use Bioreactor hardware is shipped directly from the manufacturer and will arrive crated. For unpacking instructions and detailed contents of the crate, please refer to the instructions specific to the S.U.B. volume. Be sure to follow the unpacking instructions provided and retain all packaging materials.

50 L, 100 L, 250 L and 500 L Hardware Uncrating

The S.U.B. hardware should arrive with the following items:

- Outer support container (platform, tank and control panel)
- Drive shaft, RTD, probe shelf and brackets (4) and standard tool set (spanner wrench and torque wrench)
- ETP - located on CD provided with hardware

1. Remove crate lid first
2. Remove side wall(s)
3. Remove the tie-down straps
4. Remove any/all blocks on crate floor
5. Remove S.U.B. carefully using forklift/manually by lifting via the bottom of the cart frame, not the casters
6. Ensure no damage occurred during shipping

Contact your Sales Representative immediately if damage has occurred.

1000 L and 2000 L Hardware

Detailed instructions for crating, uncrating and assembly for the 1000 and 2000 L S.U.B. units can be found in the Integrator Reference Guide.

Site Preparation

Electrical Connections

The S.U.B. hardware cannot be used on circuits equipped with GFCI circuit protection because of the potential for nuisance tripping. The electrical plug on the S.U.B. is a connector that offers a secure ground. These connectors meet the electrical safety codes for portable equipment and are International Electrical Code (IEC) rated (meet IEC standard 60309). This plug serves to provide electrical ground prior to power connection. The supplied electrical receptacle should be hardwired into the facility by a qualified electrical technician; for US installations the receptacle will require the use of an adapter mounting plate (supplied) which will fit into a 'two gang' box. For additional information on the adapter mounting plate, please see the ETP. Alternatively, the system can be hardwired directly into the facility. **NOTE:** The yellow plug and receptacle are for 120VAC and the blue are for 240VAC S.U.B.s.

Outer Support Container Preparation

Each outer support container is shipped directly from the manufacturer and arrives with various safety mechanisms in place. Please follow the guidelines below to setup the Single-Use Bioreactor upon arrival.

Warning: Any procedures that require the control box to be open should be performed with the main electrical disconnect in the locked out position and all power sources removed from the control box. For operator safety, secure the location of the S.U.B. outer support container by disabling the swivel casters before servicing. ▲

For 50 L, 100 L, 250 L and 500 L Volume Electric Resistive Heating Systems

1. S.U.B. units are shipped with the electrical breakers in the OFF position to prevent accidental activation of the heaters during hardware installation. **NOTE:** The heater should only be enabled when a liquid filled BPC is present. Using a flat head screwdriver, open the control box and locate the breakers for the PID temperature controller (middle of top row) and heater (located in middle of lower row) (Figure 1.6). These breakers should be in the upper ON position during operation. For electrical schematics, please refer to the ETP which is located on CD provided with hardware.
2. Verify position of the three-way motor controller switch–it should be in the middle position. For reference, the middle position is to enable the speed control keypad, the top position is for 0-10V controllers and the bottom is for 4-20mA controllers. Verify position of the two position temperature control toggle switch–it should be in the up position (for reference, the upper position enables the PID temperature controller).

3. Close the control box and lock the panel using a screwdriver before continuing.
4. To unlock the load cells**,** refer to Load Cell Preparation instructions below.

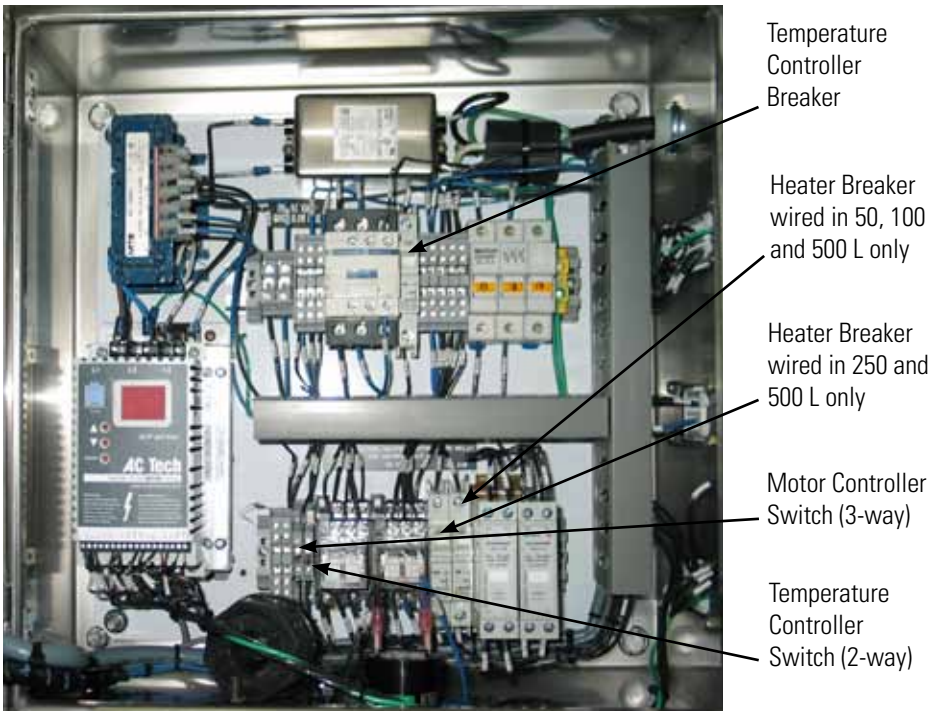


Figure 1.6 Control Box for 50, 100, 250 and 500 L Electric Resistive Heater S.U.B.

Load Cell Preparation

5. For S.U.B. hardware units purchased with factory installed load cells, the load cells are shipped in the locked position (centering washer and nut are threaded up) for equipment protection (Figure 1.7 and 1.8). A 15/16" open-box wrench is recommended for unlocking the load cells. To unlock the load cells, loosen the centering washer and nut (5/8" nut) until the nut is threaded down on the hold-down bolt about half way. Next, loosen the jam nut on the base plate until the jam nut and centering washer/nut meet. Tighten both nuts together. Using an open-end wrench, loosen the hold down bolt (by moving it upward) to provide clearance below and above the cutout in the top plate (Figure 1.61 – Section A-A). The clearance around (above and below) this nut should be from 1/8" to 3/16". Once the proper clearance has been achieved, retighten the jam nut.

Figure 1.7

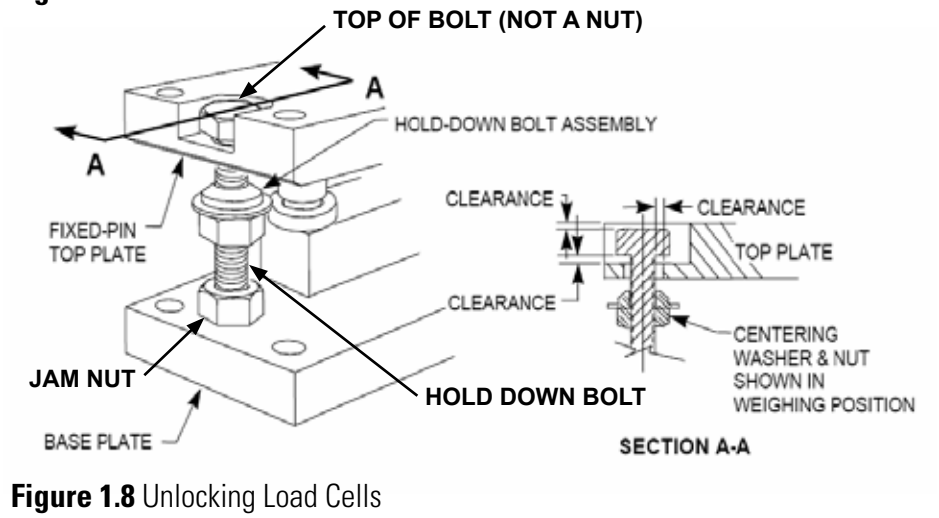


Figure 1.8 Unlocking Load Cells

6. At this point, the S.U.B. hardware is ready to be prepared for a cell culture run.
7. **CAUTION:** Do not move unit, especially when filled, while load cells are unlocked as this can damage the load cells.
8. For load cell calibration refer to Appendix C

For 50 L, 100 L, 250 L and 500 L Volume Water Jacket Systems

1. Before beginning, refer to electrical schematics included with the ETP which is located on CD provided with hardware.
2. Using a flat headed screwdriver, open the control box. Verify position of the three-way motor controller switch–it should be in the middle position (Figure 1.9).
3. Close the control box and lock the panel using a screwdriver before continuing.
4. For S.U.B. hardware units purchased with factory installed load cells, the load cells are shipped in the locked position (threaded up) for equipment protection. Refer to Load Cell Preparation instructions above.
5. At this point, the S.U.B. hardware is ready to be prepared for cell culture run.

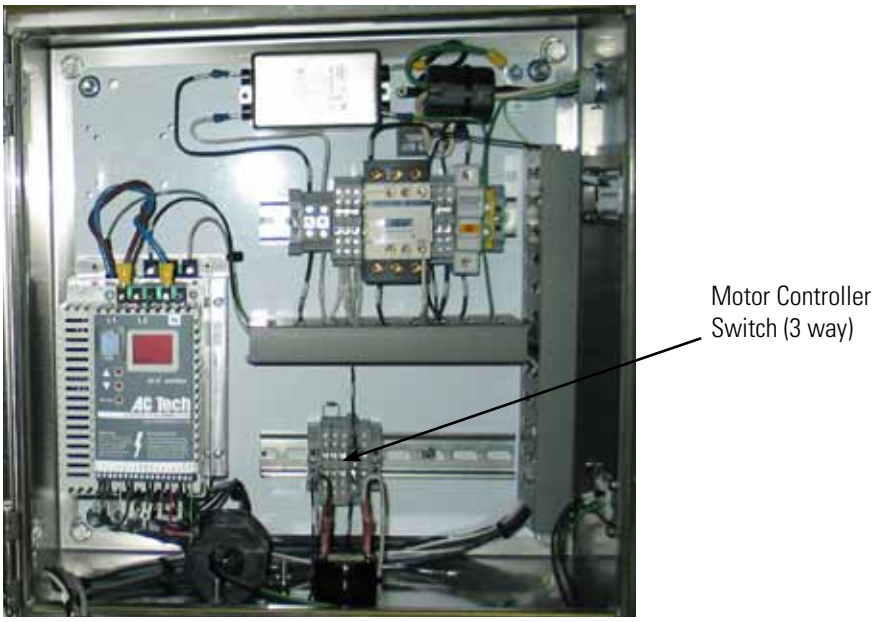


Figure 1.9 Control Box for 50, 100, 250 and 500 L Water Jacket S.U.B.

1000 L Outer Support Container Preparation

1. For resistive systems: The S.U.B. units are shipped with the electrical breakers in the OFF position to prevent accidental activation of the heaters during hardware installation. **NOTE:** The heater should only be enabled when a liquid filled BPC is present. Using a flat head screwdriver, open the control box and locate the breakers for the Proportional Integral Derivative (PID) temperature controller, heaters, pressure sensor and load cells (middle of top row) (Figure 1.10). These breakers should be in the upper ON position during operation. For electrical schematics, please refer to the ETP which is located on CD provided with hardware. **NOTE:** The heater and PID breakers are present in the Water Jacket versions, but non-operational.
2. Verify position of the three-way motor controller switch–it should be in the middle position (for reference, the middle position is to enable the speed control keypad).
3. For resistive systems: Verify position of the two position temperature control toggle switch–it should be in the up position for reference, the upper position enables the PID temperature controller.
   NOTE: This switch is present in the Water Jacket versions, but non-operational.
4. Close the control box and lock the panel using a screwdriver before continuing.

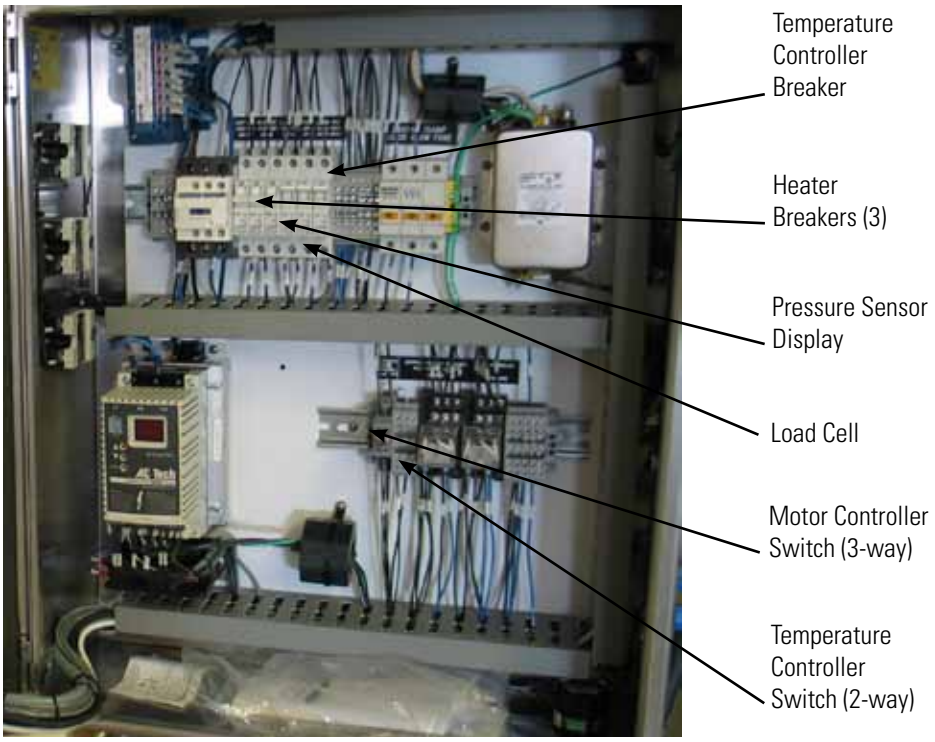


Figure 1.10 Control Box for 1000 L S.U.B. Resistive

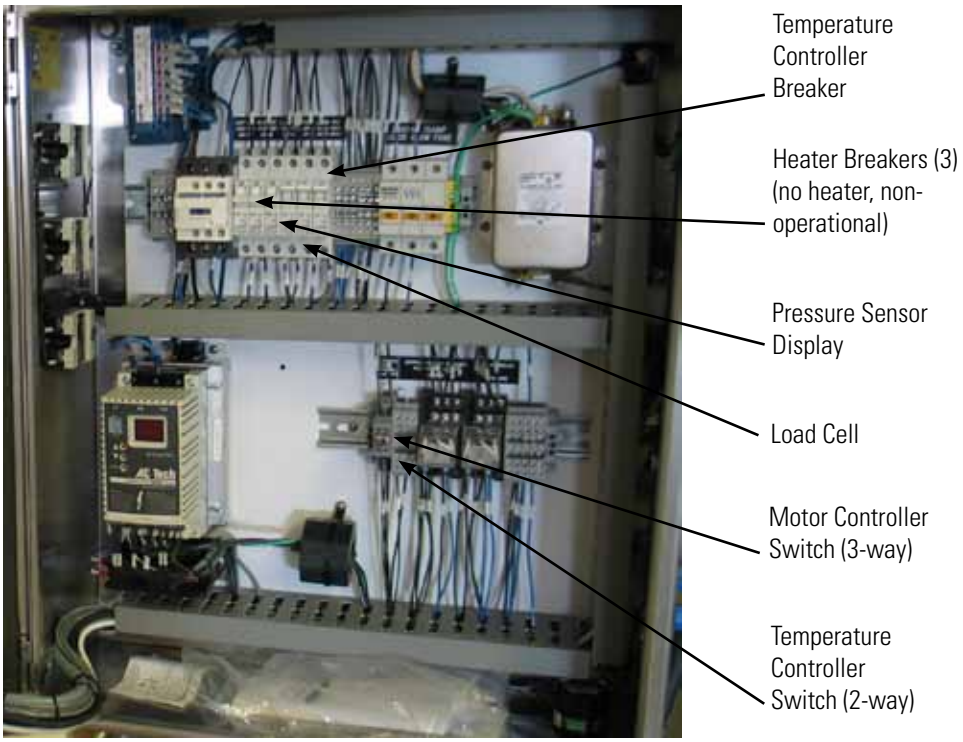


Figure 1.11 Control Box for 1000 L S.U.B. Jacketed

Load Cell Preparation

5. For S.U.B. hardware units purchased with factory installed load cells, the load cells are shipped in the locked position (centering washer and nut are threaded up) for equipment protection (Figure 1.12 and 1.13). A 15/16" open-box wrench is recommended for unlocking the load cells. To unlock the load cells, loosen the centering washer and nut (5/8" nut) until the nut is threaded down on the hold-down bolt about half way. Next, loosen the jam nut on the base plate until the jam nut and centering washer/nut meet. Tighten both nuts together. Using an open-end wrench, loosen the hold down bolt (by moving it upward) to provide clearance below and above the cutout in the top plate (Figure 1.65 – Section A-A). The clearance around (above and below) this nut should be from 1/8" to 3/16". Once the proper clearance has been achieved, retighten the jam nut.

Figure 1.12

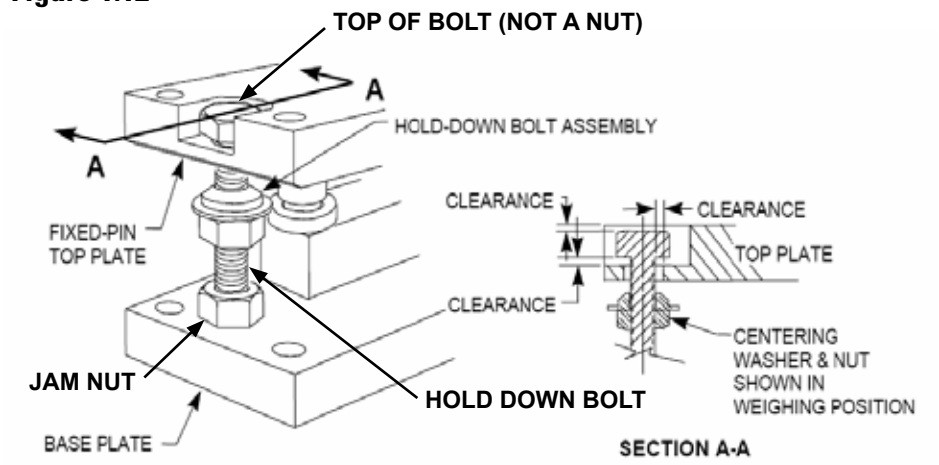


Figure 1.13 Unlocking Load Cells

6. At this point, the S.U.B. hardware is ready to be prepared for a cell culture run.
7. **CAUTION:** Do not move unit, especially when filled, while load cells are unlocked as this can damage the load cells.
8. For load cell calibration refer to Appendix C

2000 L Outer Support Container Preparation

1. Using a flat head screwdriver, open the control box and locate the breakers for the pressure sensor, continuous power outlets non E-stoppable (2), continuous power outlets E-stoppable (2) (Figure 1.14). These breakers should be in the ON position during operation (blue indicator pressed in). For electrical schematics, please refer to the ETP which is located on CD provided with hardware.
2. Verify position of the three-way motor controller switch–it should be in the middle position (for reference, the middle position is to enable the speed control keypad).
3. Close the control box and lock the panel using a screwdriver before continuing.

Load Cell Preparation

4. For S.U.B. hardware units purchased with factory installed load cells, the load cells are shipped in the locked position (centering washer and nut are threaded up) for equipment protection (Figure 1.15 and 1.16). A 15/16" open-box wrench is recommended for unlocking the load cells. To unlock the load cells, loosen the centering washer and nut (5/8" nut) until the nut is threaded down on the hold-down bolt about half way. Next, loosen the jam nut on the base plate until the jam nut and centering washer/nut meet. Tighten both nuts together. Using an open-end wrench, loosen the hold down bolt (by moving it upward) to provide clearance below and above the cutout in the

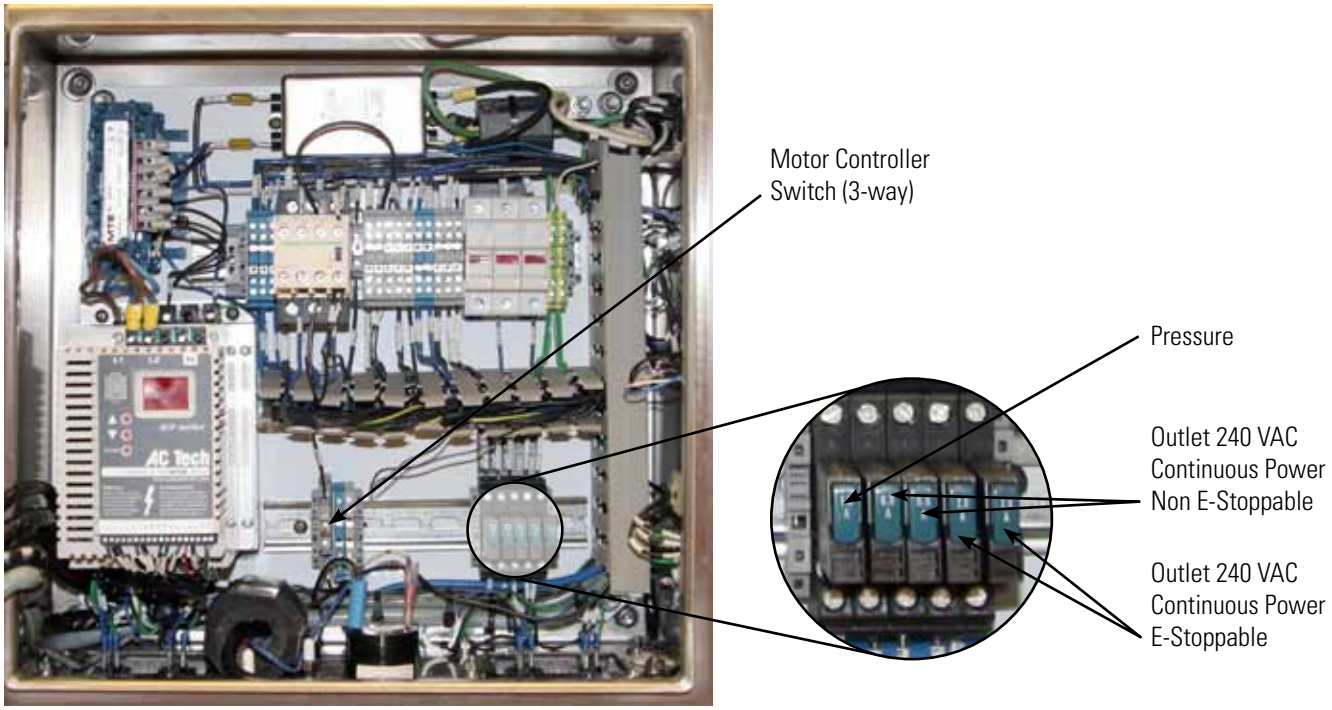


Figure 1.15 Control Box for 2000 L Jacketed S.U.B.

top plate (Figure 1.16 – Section A-A). The clearance around (above and below) this nut should be from 1/8" to 3/16". Once the proper clearance has been achieved, retighten the jam nut.

Figure 1.15.

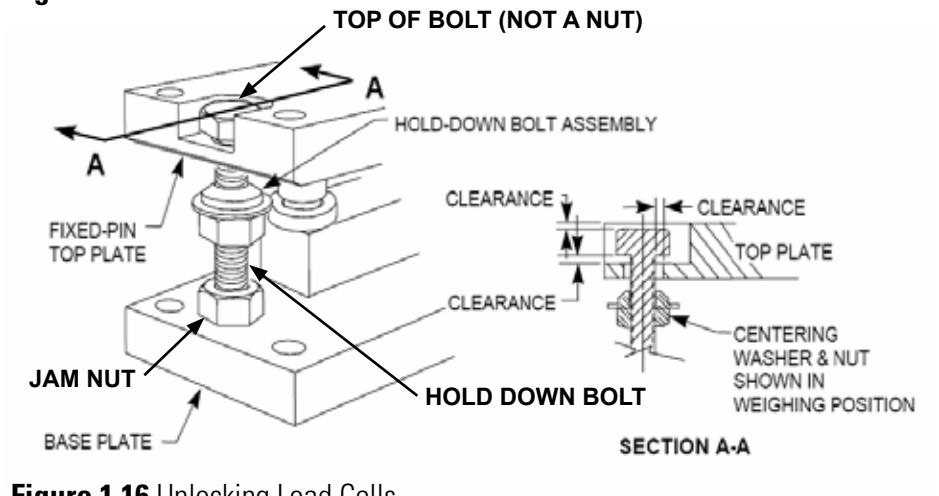


Figure 1.16 Unlocking Load Cells

6. At this point, the S.U.B. hardware is ready to be prepared for a cell culture run.
7. **CAUTION:** Do not move unit, especially when filled, while load cells are unlocked as this can damage the load cells.
8. For load cell calibration refer to Appendix C

1.7 Installation and Setup

Outer Support Container Preparation

All manual movements of mobile S.U.B. hardware (does not include 2000 L S.U.B.) should be over smooth surfaces with the S.U.B. empty and disconnected from all power and gas/feed sources. All load cells must be fully locked down. Refer to the appropriate subsection within Section 3 of this User's Guide for graphics illustrating the control panel interface for the appropriate hardware.

1. Verify facility electrical supplies are sufficient to support the power requirements of the S.U.B. and ancillary components such as controllers or pumps.
2. Locate the outer support container in the area for the cell culture run.
3. If monitoring the volume, the unit may be located on a scale if load cells are not utilized. Other applications may measure all liquids going in and coming out.
4. Level the platform by disabling the swivel casters on the bottom of the outer support container. This is accomplished by threading the leveling pads (at the center of each caster) to the floor.
5. Verify the location of the pH/DO controllers and assure cable/tubing lengths are satisfactory.

WARNING: ELECTRICAL SHOCK. ▲

6. Verify the main power is off and the emergency stop is pulled out.

NOTE: THE EMERGENCY STOP DISCONNECTS ALL POWER TO THE SYSTEM. AN ALARM BUZZER WILL SOUND WHEN THE EMERGENCY STOP IS ACTIVATED. ▲

7. Verify that the main motor power switch is in the off position.
8. Connect all electrical plugs to facility power. **NOTE:** 120 VAC - 250 L S.U.B. to be connected to a dedicated 20A circuit. Refer to hardware/electrical labels and schematics to ensure proper electrical voltage is connected to the S.U.B. The main power switch can now be turned on.
9. Resistive heating systems - Verify the temperature controller is off (the display should be flashing in the standby position).
10. Water Jacket Systems - Connect water inlet and outlet lines from temperature control unit quick connects to the jacket (Figure 1.17). For 50 L through 500 L and 2000 L S.U.B. systems, the inlet is typically on the left side if facing the connectors. For the 1000 L S.U.B., the inlet is the lower connection and the outlet is the upper.

Figure 1.17 Water Jacket Connection

Figure 1.18 Frit Spage line holder

Air Line Preparation

See Table 1.6 for recommended flow rates. The operating pressures at the level of the S.U.B. are of primary importance and these values must be adhered to. Please note flow rates in the graphics include both half and full volume applications.

Porous Frit Sparge

If you will be using a porous frit sparge in your S.U.B. bag, whether alone or in a dual sparge setup, we recommend using the frit sparge line support (Figure 1.18) for S.U.B. sizes 250 L and smaller. Simply attach this line support underneath the tank directly below where the porous frit sparge will be placed. This support piece holds the sparge gas tube vertically so that the frit sparge itself is oriented in the vertical position for maximum sparge effectiveness. Spring-loaded screws permit a simple sliding of the holder clip onto the tank bottom. With the frit sparge holder attached to the tank, the sparge line can be wound through the coil of the holder to keep the sparge oriented properly.

WARNING: The S.U.B. BPC is not rated as a pressure vessel. The BPC should not be allowed to become tight during inflation or operation. Gas pressure in the BPC should not exceed 0.5 psi (0.03 bar) at any time. Conditions of over pressure may result in BPC damage or personal injury. For reference the BPC will appear to be tight at 0.1 psi (0.007 bar). ▲

1.8 S.U.B. Operation Information

BioProcess Container Preparation and Loading

Each outer support container is designed for a specific Single-Use Bioreactor BPC. Confirm the correct volume BPC is being used for the corresponding volume outer support container. Sections 2.3 and 2.4 outline the installation and setup of the different volume S.U.B. BPCs–please adhere to these instructions in the order in which they are presented.

BPC Handling Instructions

Take care if using a sharp object when opening outer polybags to avoid damaging the S.U.B. bag. When placing bags in containers, do not drag bag over corners or sharp objects. Do not lift the bag by the corners or top seams. Carefully coil tubing on top of bag to prevent puncturing bag with cable ties or clamps. Use cushioning between tubing and bag in storage and transport.

BPC Operating Information

Aseptic Line Connection

The most common recommended process for making connections to the tubing lines is with an aseptic tubing fuser such as those in Table 1.4.

NOTE: Other connection options are available as a custom S.U.B. BPC assembly.

Following the recommended tubing welder operating instructions, successful connections can be obtained for filling, supplementing, sampling, or dispensing from the S.U.B. BPC as needed.

Commonly Used Tubing Welders for Aseptic Connections			
Brand	**Model/die set**	**Tubing Size ID–OD**	**Tubing Material**
Terumo	SCD-IIB (std)	1/8 - 1/4" (3.18 - 6.35 mm)	C-Flex
Wave	STF-IRc (1/4" [6.35 mm])	1/8 - 1/4" (3.18 - 6.35 mm)	C-Flex
Wave	STF-IRc (7/16" [11.11 mm])	1/4 - 7/16" (6.35 - 11.11 mm)	C-Flex
Wave	STF-IRc (5/8" [15.88 mm])	3/8 - 5/8" (9.53 - 15.88 mm)	C-Flex
Wave	STF-IRc (3/4" [19.05 mm])	1/2 - 3/4" (12.7 - 19.05 mm)	C-Flex

Table 1.4 Some tubing welders for S.U.B. aseptic connections

Working Volume

Each S.U.B. is designed for a working volume range. The minimum working volume and the rated working volume are listed in the specification table (see Section 3). The total volume listed includes the headspace needed for proper aeration and gas management. **Actual working volumes should not exceed the indicated rated working volumes by greater than 10 percent. In addition, working volumes less than 50 percent of the rated volume can result in damage to the S.U.B. BPC and hardware.**

Aeration

The standard S.U.B. bag is designed with special spargers that produce very efficient mass transfer of oxygen and typically will require much less gas inflow than conventional spargers. Gas inflow, in fact only need be limited to prevent foam generation and excessive pressure within the BPC. Gas flow rates supplied as overlay should also be reduced as much as possible or eliminated; this will minimize both liquid evaporation and demand on the exhaust filter. Ideally this will reduce the likelihood that gas inflows will exceed gas outflow of the system and reduce the occurrence of foam in the headspace that may plug the exhaust filter.

Exhaust vent filter

The exhaust vent filter used on the 50 L - 1000 L S.U.B. is a Pall KA3 series filter utilizing hydrophobic PVDF membranes. These filters can be oriented in two directions 1) normal orientation with the flow arrow on the filter housing pointing away from the BPC and 2) reverse orientation with the flow arrow pointing toward the BPC. In the normal orientation, the filter has the maximum filter capacity; however the side-vents are positioned on the sterile side of the membrane. Condensate removal in this orientation requires the use of a vent filter heater. If the orientation is reversed, the filter capacity is reduced slightly; however, the side-vents are now on the non-sterile side, allowing condensate to be removed with a syringe (vent heater is optional). The standard S.U.B. BPC is supplied with the filter in the reversed orientation. **NOTE:** If normal orientation is desired, this must be specified upon ordering and is considered a custom request. It is important during operation the filter media be free of condensate in order to maximize the capacity of the vent filter.

To drain the condensate from the outer housing of the vent filter, do the following:

1. Turn the molded fitting of the lower side vent counterclockwise.
2. Twist the side vent back and forth slightly to release the seal on the O-ring inside the side vent.
3. Attach a needleless luer lock syringe to the lower side vent and remove the condensate.

For users with more demanding applications, an optional vent filter heater can be used (see Section 5.3 for filter heater ordering information).

The exhaust vent filters used on the 2000 L S.U.B. are Meissner UltraCap series filters utilizing hydrophobic PVDF membranes. These filters are provided in normal orientation with the flow arrow on the filter housing pointing away from the BPC. In the normal orientation, the filter has the

maximum filter capacity. No side vents are provided; condensate must be managed by use of the condenser system or vent filter heater.

Sampling

The S.U.B. is equipped with a small volume sample port that is part of the S.U.B. BPC thermo-well. This small diameter (1/16 x 3/16" [1.59 x 4.76 mm]) silicone dip tube of 6" (15.24 cm) length allows low void volume samples to be taken for cell viability and density, as well as analyte analysis. This dip tube is supplied with an aseptic luer lock connector (SmartSite) that allows for direct sampling or attachment of various sampling manifolds by use of standard luer lock connection. Alternatively, manifolds can be welded onto the C-Flex sample line (1/8 x 1/4" [3.18 x 6.35 mm]) by tubing welder. For recommended systems for fluid transfer, see data sheet 016 (contact your sales representative for a copy).

WARNING: Gas pressure within the S.U.B. BPC headspace **should not exceed 0.5 psi (0.03 bar) at any time**. Conditions of over pressure may result in BPC damage or personal injury. ▲

Operating Pressure

The S.U.B. BPC is not operating as a closed system, as it has both inlet and exhaust filters that are utilized to maintain a sterile environment for cells to grow without concern for contamination. However, conditions can be encountered when gas inlet flow rate may exceed exhaust flow rate. This may be encountered in the unlikely event of the failure of a pressure regulator on a gas feed, or when excessive foam within the bioreactor creates conditions of vent blockage. The S.U.B. BPC is not rated as a pressure vessel. All gas supplied to the bioreactor controller must be regulated to a pressure not to exceed manufacturer's recommendations (typically 10 psi (0.69 bar). Gas pressure in the S.U.B. BPC headspace should not exceed 0.5 psi (0.03 bar) at any time.

- More demanding applications may warrant an optional exhaust vent heater (See Section 5.3).
- If foaming is excessive in your cell culture process, it is best to reduce the operating volume of the process to 80% of maximum rated working volume of the S.U.B. system being used to provide greater head space volume.
- Disposable pressure transducers are available on custom S.U.B. configurations and are standard on the 1000 L and 2000L systems. This technology combined with high-level control systems common with industrial applications can regulate gas pressure within the confines of the S.U.B.

Extensive cell culture testing has not found an occurrence of overpressure sufficient to create a containment breach. Development testing of the S.U.B. BPC system has shown that in conditions of excessive pressure the polymer bag will fail at the upper regions of the chamber where it is unsupported by the outer support container, minimizing the likelihood of the loss of bulk liquid.

Agitation

The agitator should not be operated at volumes less than the stated minimum volume. Stirring speed is adjusted by using the keypad interface on the control panel. The agitation control interface utilizes a red LED digital display to indicate stirring speed in units of revolution per minute (RPM). Power is supplied to the motor by a two position power switch that is illuminated in green when turned to the ON position (right position). The up and down arrows on the agitation keypad adjust the stirring speed. Due to the auto-restart capabilities of the S.U.B., the green start button on the keypad has been disabled; however the red stop button on the keypad is active. If the red stop button has been used to stop the motor, the controller can be reset and agitation restarted by using the main motor toggle switch on the left side of the control panel.

Dispense and Harvest

The S.U.B. is equipped with a bottom drain line that allows for liquid harvest by means of peristaltic pump. Connection of the bottom drain line can be accomplished by use of a tubing welder or the aseptic connection of 1/4" - 3/8" (6.35 - 9.53 mm) quick connect that is provided. For S.U.B.s 50 L to 1000 L, the bottom drain exits the S.U.B. BPC at the lowest vertical position on the side of the S.U.B. This allows for easy access for the user and minimizes the accumulation of cells in the area of the drain during the cell culture run. Manipulation of the S.U.B. BPC as the last few liters of media drain will minimize liquid hold-up within the S.U.B. The 2000 L S.U.B. is provided with a 1" style bottom drain near the center line of the tank bottom.

Hardware Operating Information

Temperature (Electric Resistive Heating Systems)

Temperature setpoints can be adjusted via the temperature controller located on the front panel of the S.U.B. control box. This controller is preprogrammed to avoid overshoot during heat up and maintain a target temperature of +/- 0.5°C based on the set value (SV) display (green LED). (The set value of the PID temperature controller is factory preset at 2°C to prevent premature heat up). The process temperature is measured by means of a supplied RTD (pt-100) that is inserted into the thermo-well of the S.U.B. BPC. The temperature measured by the RTD is displayed with a red LED digital display as the present value (PV). For more detailed operating information on the controller, refer to the ETP.

- Enable/disable temperature controller by pushing left button.
- Adjust temperature set value by pushing up and down arrows located on the right.
- Process temperature value is illuminated in red.
- Flashing numeric display indicates the controller output is off (standby mode).

NOTE: The heaters are not enabled unless the motor agitation is operational and should not be engaged until the BPC is filled to at least the minimum volume. ▲

Heating Performance

Heating times for the Single-Use Bioreactor systems vary based upon liquid volume and temperature, ambient or heating liquid temperature, sparge rate and mixing rate. Users should adjust process liquid staging and seeding strategies to the unique aspects of the S.U.B. Process controllers and heaters are designed to provide optimum heat transfer and to minimize heat up times, while maintaining the material integrity of the polymer film construction of the S.U.B. BPC. (see Table 1.5)

Do not operate heater if S.U.B. BPC is not at minimum liquid volume or greater. Care must be taken not to melt or damage the bag or other disposable components of the S.U.B. BPC. Heaters should not be used to warm liquid above 40°C. In order to reduce the possibility of the tank becoming too hot, the heaters are supplied with a thermostat that will limit temperature to 65 +/- 5°C. The main power disconnect should be in the off position unless the S.U.B. hardware system is in active use. This will preserve the long term reliability of the heating system.

Note: Users can reduce the heating time required to warm media by allowing media to warm to ambient temperatures before transferring into the S.U.B. BPC.

WARNING: The heating element is provided with an over-temperature safety that will prevent direct damage of the heater element. **The heater must not be operated when the outer support container is empty or when the S.U.B. is below minimum liquid operating volume. Serious harm to the operator or damage to the S.U.B. BPC will result. ▲**

General temperature mapping has been performed for the S.U.B. systems by tracking thermal profiles within the liquid confines of the bioreactor. Testing conditions were analyzed using chilled media and low agitation rates. Gradients within the liquid did not exceed 0.5°C during heat up. Testing has also shown that temperature measurements in the S.U.B. when using the standard silicone thermo-well with 1/8” (3.18 mm) diameter temperature probes property represent bioreactor content temperatures. Users desiring exact temperature calibrations can order S.U.B. temperature/sample port (See Section 3.9). Using this port will allow users to simulate the temperatures seen by the RTD when used with the S.U.B. BPC.

Heating Times for S.U.B. systems (ambient temperature of 25 °C - values for jacketed systems assume a TCU heater size of 10W per batch liter)				
System	**Liquid Batch Volume (half/full)**	**Initial Liquid**	**Liquid Target**	**Time (half/full)**
Electric 50 L	25 L (minimum) / 50 L	5°C	37°C	5 hrs / 7.5 hrs
Jacketed 50 L	25 L (minimum) / 50 L	5°C	37°C	3 hrs / 2.5 hrs
Electric 100 L	50 L (minimum) / 100 L	5°C	37°C	5 hrs / 7.5 hrs
Jacketed 100 L	50 L (minimum) / 100 L	5°C	37°C	3.3 hrs / 3 hrs
Electric 250 L	125 L (minimum) / 250 L	5°C	37°C	6 hrs / 8.5 hrs
Jacketed 250 L	125 L (minimum) / 250 L	5°C	37°C	3.5 hrs / 3 hrs
Electric 500 L	250 L (minimum) / 500 L	5°C	37°C	8 hrs / 11 hrs
Jacketed 500 L	250 L (minimum) / 500 L	5°C	37°C	3.5 hrs / 3 hrs
Electric 1000 L	500 L (minimum) / 1000 L	5°C	37°C	9 hrs / 12 hrs
Jacketed 1000 L	500 L (minimum) / 1000 L	5°C	37°C	4 hrs / 3.5 hrs
Jacketed 2000 L	1000 L (minimum) / 2000 L	5°C	37°C	4 hrs / 3.5 hrs

Table 1.5 Approximate heating times for the S.U.B.

Protective Earthing

Protective earthing for the S.U.B. hardware system and controller is provided through the ground terminal of the plug providing power. Source power to the controller must provide protective earthing to this terminal in order to minimize the hazard of a possible shock in the occurrence of a fault condition. Please refer to Appendix A.

Replaceable Fuses

Electrical components of the S.U.B. are equipped with circuit protection. The variable frequency drive used to power the mixer motor is protected by the use of midget quick blow fuses (Ferraz-Shuwmut, 10A for 50, 100 and 250 L - #OTM10 and 15 A for 500 L, 1000 and 2000 L - #OTM15). Other components of the resistive heating system, such as the temperature controller and heating element, are protected with resetable breakers. In the case of an electrical fault condition, these safety devices are designed to protect the user from electrical shock and prevent electrical system components from being damaged. Fuses can be replaced and/or the breakers reset once the fault condition is resolved.

NOTE:

- The normal “on” setting for these breakers is in the “up” position.
- A tripped breaker will be in the “mid” position.
- “Off” is in the fully down position.
- To reset a tripped breaker it must first be moved from the tripped or mid position to the off or fully down position before moving it the fully up or on position.

Scales and Weighing Systems

Monitoring liquid volume within the S.U.B. during operation can be critical in cell culture applications that involve nutrient media feeds. This can also be a useful method for increasing the scalability of the S.U.B. by starting the process run at minimum operating volume. The ability to track operating volume by use of load cells or weigh scales allows the user the ability to control liquid volume and cell density as the bioreactor is increased to rated working volume during the process run.
Load cells come standard on 1000 L and 2000 L S.U.B.s. An option available for S.U.B. volumes of 50 L to 500 L is a load cell kit for weight/volume measurement. Load cell kits can be installed at the factory or can be added later by a certified service technician. The load cell kit comes with three load cells, summing block, wiring and display with a choice of several interfaces. For more information, refer to Section 3 for ordering information. **Please ensure that load cells are locked down for any movement of the S.U.B. unit.** Refer to Section 1.6 for proper load cell operation and care, and to Appendix C for load cell calibration instructions.

Digital display weighing scales can be sourced from manufacturers such as Mettler-Toledo. Bench top scales are commonly used to measure the amount of bulk source media stored in a smaller volume BPC as it is transferred by peristaltic pump into the S.U.B. Floor scales can be used to measure the fluid content within the S.U.B. This is accomplished by rolling the S.U.B. onto the scale platform and leveling the S.U.B. skid once in position. Refer to Section 3 for skid dimensions for scale sizing.

Advanced Control Information

External Data Logging and Control

The S.U.B. hardware systems are designed to allow advanced users to control all aspects of the operation of the bioreactor. Contact technical support for Thermo Scientific HyClone products general integration guidance.

1.9 S.U.B. Operating Instructions

Checkpoints prior to Media Fill

Verify the following before proceeding to liquid fill:

√ Load BPC into hardware following instructions provided in Section 2.

√ All Kleenpak Connector port heavy duty clamps (SV20664.01 or .02) are closed and located as close as possible to the S.U.B. BPC.

√ Exhaust filter is upright and secured using the holder.

√ Clamp on drain tube is closed and located as close as possible to the S.U.B. BPC.

√ Temperature RTD is completely seated in the thermo-well and secured.

√ Air filled bag is properly oriented in the outer support container and BPC bottom tabs are secured.

Operating Conditions for Cell Culture Applications

Operating parameters for cell culture vary greatly between cell lines and media formulations. Table 1.5 is provided as a reference for establishing initial control settings for the S.U.B. Proper management of gas flow rates is a critical parameter when performing cell culture in a BPC. It is therefore recommended the end user carefully consider the gas flow rate introduced into the S.U.B. The gas flow rates listed here are recommended maximum rates. If the oxygen demand of the culture exceeds that delivered by these rates, the gas ratios can be adjusted accordingly to deliver more oxygen.

- It is strongly recommended not to exceed the total maximum gas flow rate into the bag. Otherwise, these high sparge flow rates will result in excessive foaming and increased load on exhaust vent filters.
- A sparge strategy that uses an initial flow rate of air and then cascades supplemental oxygen has been shown to be a highly effective approach in maintaining the desired oxygen saturation setpoint. This is typically the most efficient strategy for meeting the respiration demands of high density cell culture while reducing the risk of creating excessive pressure in the S.U.B.

Lower flow rates provide two important benefits: 1) reduced generation of foam in the headspace area and 2) reduced pressure loading on the S.U.B. BPC and exhaust vent filter. When using oxygen cascade, flow rates can typically be reduced four to five times as compared to air because air typically contains less than 20% oxygen per unit volume.

Table 1.6 below contains a listing of gas outlays for all sizes of S.U.B.s to be used in specifying maximum gas flow rates for mass flow controllers or rotameters. In optimal conditions (no condensation or fouling) the

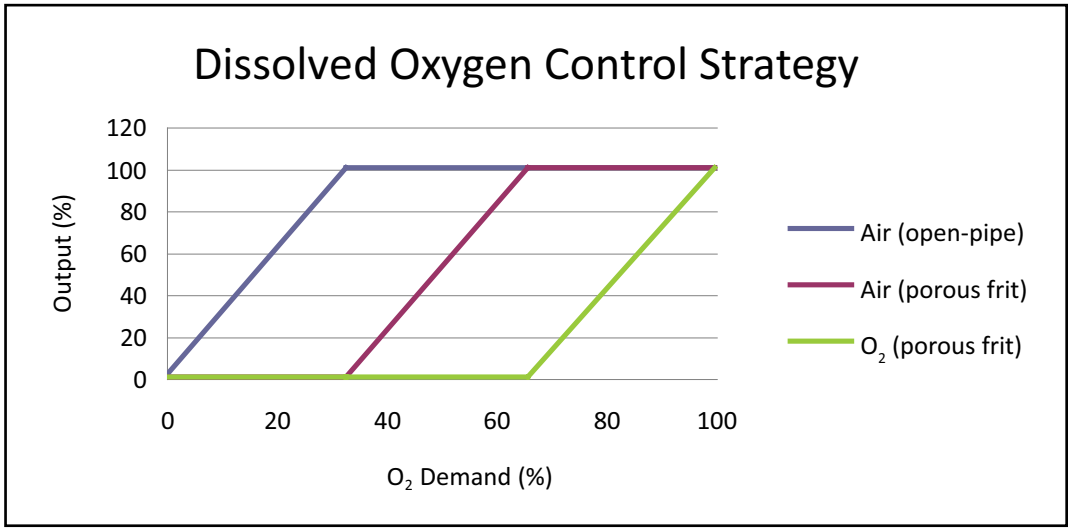
exhaust filters have a flow capacity of at least 20 lpm at 0.1 psi. The total flow rate of gas into system must be less than 20 lpm per active exhaust filter. The values listed take into account the number of exhaust filters that are standard on each size of S.U.B. (1 installed for the 50, 100 and 250 L and 2 installed for the 500 and 1000 L). The components of 2000 L system are scaled up to allow flow ratings of 50 lpm at 0.1 psi. These values are a good rule of thumb, but are not absolute requirements. They are also not intended to be process gas flow settings. The process gas flow settings should be adjusted as discussed below with starting conditions not exceeding 50% of the listed max values (this will help avoid accidental foam-out of the S.U.B. exhaust filter).

S.U.B. Range of Operating Parameters																		
	50 L			100 L			250 L			500 L			1000 L			2000 L		
Operating Volume (L)	25-50			50-100			125-250			250-500			500-1000			1000-2000		
Agitation Rate (rpm)	30-200			30-200			30-150			30-150			20-110			20-75		
Temperature (°C)	2.0 - 40.0 ± 0.1																	
Recommended Max. Gas Flow Rates	Open Pipe	Frit	Overlay	Open Pipe	Frit	Overlay	Open Pipe	Frit	Overlay	Open Pipe	Frit	Overlay	Open Pipe	Frit	Overlay	Open Pipe	Frit (3)	Overlay
Air (lpm)	1	0.5	5	2	1	10	5	2.5	10	10	5	15	10	8	15	12	16	15
O_2 (lpm)	-	0.25	-	-	0.5	-	-	1.25	-	-	2.5	-	-	4	-	-	8	-
CO_2 (lpm)	-	0.1	-	-	0.2	-	-	0.5	-	-	1	-	-	1	-	-	1	-
N_2 (lpm)	-	0.25	-	-	0.5	-	-	1.25	-	-	2.5	-	-	2.5	-	-	2.5	-

Table 1.6 Operating Conditions for Cell Culture Applications (Full and half volume)

Gas Supply Setup

The following graph depicts a dissolved oxygen management strategy. Refer to Table 1.6 for actual gas flow rate recommended maximum values.



Graph 1.1. Dissolved Oxygen Control Strategy

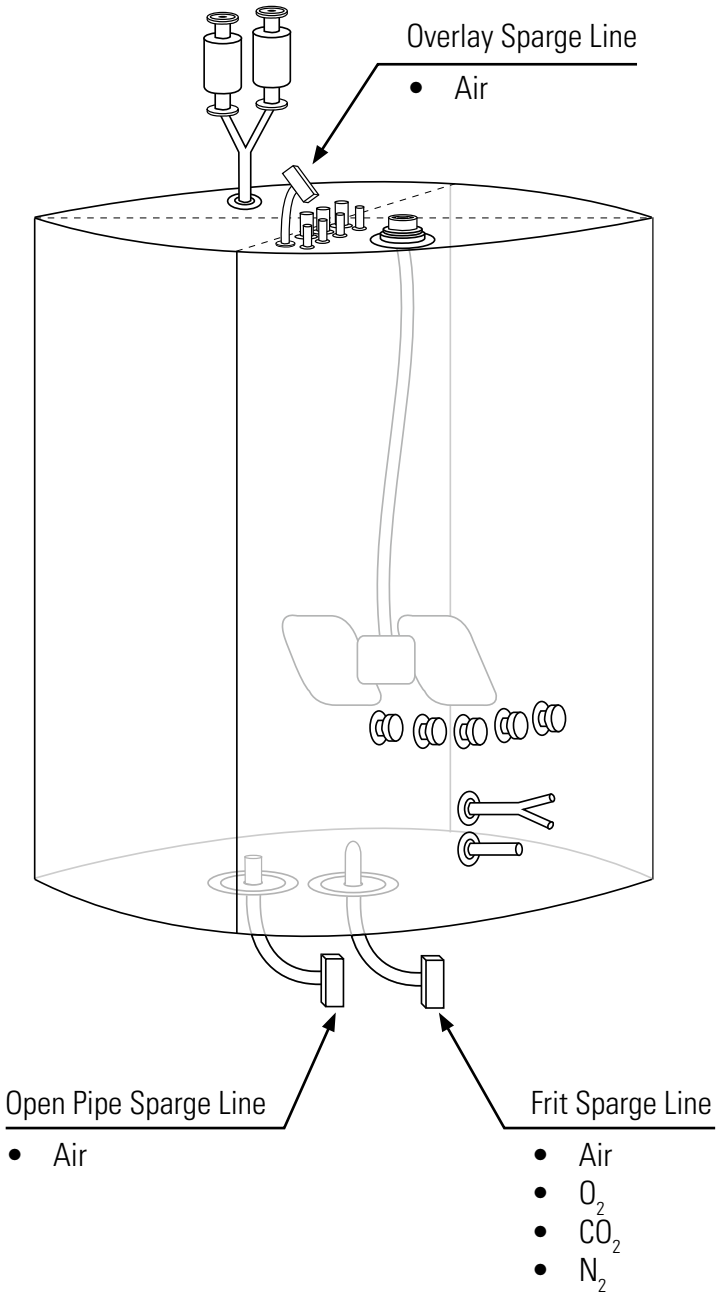


Figure 1.19 Recommended Gas Inflow Setup

In developing the gassing strategy for the dual sparge S.U.B. bag it is recommended that a cascade system be used to maintain dO_2 setpoint starting with the open-pipe only (air ramping from 0 to 100% output), then cascading to air to the frit (ramping from 0 to 100% output) when needed, then finally O_2 to the frit. This strategy has allowed excellent CO_2 stripping and high O_2 delivery for high cell densities with little foam formation. The cell culture medium used may vary these results (refer to Graph 1.1 and Figure 1.19).

For more information on growth of specific cell lines in the S.U.B. system, please contact technical support.

Media Fill

1. Select desired line set from the S.U.B. BPC for fluid introduction.
2. Make aseptic connection (tubing welder, quick connect or tri-clamp) and begin liquid fill.
3. Once approximately 20-30 L of volume has been added, verify the position of the BPC in the outer support container, particularly the sparger and the drain line. Adjust positioning if necessary for proper fit.
4. It is recommended that the top corners of the BPC be pulled upward to reduce wrinkles during filling. **NOTE:** The BPC must be pulled at the top corners as the bag will generally form wrinkles during liquid fill. If the film is not pulled from the top to remove wrinkles, film tensioning below the bearing port will result.
5. The stretch hooks can be removed from bottom corners of the S.U.B. BPC when fluid volume reaches 30% volume. This will eliminate any interference with the load cell readings.
6. Fill to desired liquid volume — 50%-100% of rated volume is recommended.
7. If employing a liquid batch-to-tank grounding cable with the stainless steel connector of the sample line, the sample line should be purged of air prior to probe calibration.

Agitation

1. Once the media has reached half volume of the S.U.B., the agitation control can be turned on via the motor ON/OFF switch.
2. Using the arrow keys, adjust the setpoint speed to the desired level (the red LED display indicates the stirring speed in RPM). Adjust desired agitation rate within the recommended range per Table 1.6.
3. Allow speed to stabilize, then make fine adjustments if necessary.

NOTE: Agitation must be stopped when volume falls below minimum (1/2 of the rated volume), otherwise damage to the hardware or disposable components may result. ▲

Temperature Control (Electric Resistive Heating Systems)

1. After the agitation has been set, turn on the temperature controller via the temperature controller keypad (left button). A flashing numeric display indicates the controller is off (standby mode).
2. Adjust temperature set value using the up and down arrows located to the right.
3. The process temperature value is shown in red.

Temperature Control (Water Jacket Systems)

1. Connection to an external temperature control unit (TCU) is made via the large quick connect couplings located on the vessel jacket. Ensure the inlet/outlet ports are connected properly; improper installation may result in poor heating/cooling performance.
2. Jacket should be purged of air any time the vessel jacket lines are reconnected.
3. Temperature set points are controlled by the TCU. Refer to the TCU manufacturer's guidelines for setup and operating instructions.

Drive Shaft Rotation

Verify rotation of the drive shaft is operating in a counterclockwise motion when viewed from the top looking down. The S.U.B. is designed to mix in this direction only.

pH Probe Calibration

In general, the pH probe calibration (post-autoclave) can be verified by pulling a sample and analyzing the pH on another calibrated pH meter.

DO Probe Calibration

After polarizing for 6 to 8 hours, the DO probe can be calibrated in the S.U.B. using standard protocols. In general, turn on full air sparging (do not exceed 1 lpm in 50 L, 1 lpm in 100 L, 2 lpm in 250 L, < 4 lpm in 500 L, <6 lpm in 1000 L, or <10 lpm in the 2000 L) until the DO reading stabilizes; this is 100% DO setpoint for the controller. A zero percent dissolved oxygen setpoint can be achieved by sparging with nitrogen or by unplugging the DO probe momentarily.

Checkpoints Prior to Inoculation

Verify the following before inoculation:

√ Once S.U.B. is filled with media, disconnect BPC tabs from the S.U.B. hardware.
√ Verify temperature and agitation are at the desired setpoints.
√ pH probe is calibrated, autoclaved and connected via a Kleenpak Connector port.
√ DO probe is autoclaved, connected via a Kleenpak Connector port, polarized (6 to 8 hours) and calibrated.
√ Temperature RTD is completely seated in the thermo-well and secured.
√ A method for making aseptic tubing connections should be available.

Cell Inoculation

Once the S.U.B. is operating at the targeted steady equilibrated state and has achieved temperature, the S.U.B. is ready for inoculation. Connect the inoculum addition line set to the seed culture vessel (equipped with the proper connectors/tubing) and transfer the inoculum into the S.U.B. Typically this is done with the tubing connection process (aseptic luer lock connection or tube welding) and peristaltic pump. Pump the desired volume of seed cells into the S.U.B. **NOTE:** For shear sensitive cultures, cells can be introduced by manipulating the addition port to direct the inoculum down the interior wall of the BPC and into the bulk fluid, reducing the shear on the cells. Custom line sets can be supplied with dip tubes which shorten the distance between the point of inoculum introduction and the bulk fluid level.

Checkpoints In-Process

Verify the following once or twice daily during the culture run:

√ Visual verification of sparging (rising bubbles) through the sparge access window.
√ Verification of process parameters such as temperature and agitation are at setpoint.
√ Bag is not operating under pressure.
√ Cap is tight on drive shaft.
√ Temperature RTD is completely seated and secured.
√ That no condensate accumulates in exhaust filter housing. If condensate has accumulated then this indicates that use of a filter heater or a Condenser System is required.

NOTE: Noise may be emitted from the mixer assembly during operation. This noise may vary in intensity and frequency, but generally has no significant effect upon performance or overall durability of the S.U.B. BPC during the intended life of the product. ▲

Dispense and Harvest

1. Connect bottom drain tubing set to intended transfer line.
2. Open clamp positioned at the bottom drain port.
3. Begin drain by use of peristaltic pump.
4. When approximately 3-5 liters remain in the S.U.B. BPC, lift the S.U.B. BPC at the top hanging tabs located opposite of the bottom drain (this will pool media towards drain).
5. Hold bottom drain line near floor while lifting exhaust filter side of S.U.B. BPC to facilitate the drain of the final liter of harvest media.

S.U.B. BPC Disposal

Once the S.U.B. is drained, the drive shaft can be removed and stored by reversing the steps used during assembly. The S.U.B. BPC can then be removed from the outer support container. Filters can be removed and integrity tested as needed as per user's standard procedures. All product contact materials related to the S.U.B. can be disposed of in an appropriate waste container or incinerator.

S.U.B. Shutdown

1. Once run is complete, verify motor agitation is off and turn off the power to the outer support container by switching off the main power disconnect.
2. If the S.U.B. hardware has come in contact with caustic materials during the course of a run, rinse affected areas with a light water rinse, followed by normal routine cleaning (see Preparation for Next Run section).
3. Loose items such as the drive shaft, tools and RTD probes should be returned to their storage locations to prevent accidental damage.

Preparation for Next Run

Between runs, the S.U.B. hardware (outer support container, probe shelf, drive shaft and mixer drive, etc.) can be wiped down with sanitary wipe. The outer support container can also be cleaned with typical stainless steel cleaner. Store drive shaft in storage holder located near the handle of the outer support container.

The S.U.B. hardware system can be cleaned to the extent of standard laboratory cleaning procedures. Care should be taken to ensure electrical connections have been disconnected and electrical enclosures are closed tightly. It is also recommended that excess water is not introduced under the heat shield or over the control panel. A wipe down with normal disinfectant solutions is sufficient, but without using excessive amounts of liquid. The unit must be allowed to fully dry prior to being brought back into operation.

Routine Maintenance

Environmental conditions, operating parameters and the ability of the user to adhere to standard operating procedures as outlined in this User's Guide can have significant impact upon the useful life of the S.U.B. hardware system. The following guidelines are based upon standard operating conditions as outlined in the S.U.B. User's Guide.
High wear items such as bearings, seals, O-rings, and sterilization valves common to conventional bioreactor systems have been purposefully considered in the design of the disposable construction of the S.U.B. The S.U.B. system is inherently robust and requires low levels of routine maintenance. Taking time between bioreactor runs to clean the exterior of the S.U.B. is certain to improve the appearance and overall longevity of the hardware system. The drive motor is industrial grade induction motor with permanently sealed and lubricated gear box.
The drive shaft is constructed to wear slightly with use and should be visually inspected after each run. The heating elements are designed to operate well within manufacturer's design limits and will provide years of consistent performance. Visual inspection of wear components and following the guidelines listed below will be sufficient to ensure years of dependable service. Replacement parts are available (refer to Section 4.4 for information).

Preventive Maintenance Schedule

Replace drive shaft assembly after one year of service or refer to the following wear specifications:

- Refer to the Table 1.7 for new drive hex diameters and minimum drive shaft head hex diameters. Diameters are measured at widest location across the points. Replace worn shaft head assembly when drive hex diameter at widest location measures equal to or less across the points (Figure 1.20).
- Lightly coat drive cap threads with food-grade anti-seize if cap becomes difficult to turn.
- Replacement of the drive motor and heater element is recommended after two years of service.

S.U.B. System	New Hex Diameter	Minimum Hex Diameter
50, 100 and 250 L	0.587"+/- 0.005" [14.9 mm]	0.566" [14.4 mm]
500 and 1000 L	0.839" +/- 0.005" [21.3 mm]	0.820" [20.8 mm]
2000 L	Replace after 1 year of service (mandatory).	

Table 1.7 Shaft head dimensions

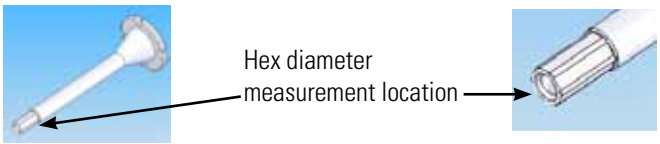


Figure 1.20 Shaft head assembly

Section 2 Operating Information

This section covers the following:

2.1 Calibration Procedures

Mixer Speed Calibration

To verify the calibration of the mixer speed, use a calibrated tachometer. Expect accuracy of +/- 1 rpm. Speed scaling can be modified if the calibration needs to be adjusted. Please refer to Section 3.6 for details.

Temperature Controller Calibration

To verify the calibration of the temperature controller/RTD, use a S.U.B. silicone thermo-well, the existing 1/8" OD RTD and a user supplied calibrated temperature bath.

Pressure monitor Calibration (when present)

To verify the calibration of the pressure monitor, use a calibrated pressure standard. Pressures can be verified by clamping the BPC inlet line and supplying gas through the overlay gas filter. Expect accuracy of +/- 0.1 psi. The monitor can be calibrated manually by referencing the monitor operator's manual supplied in the ETP.

Load Cell Calibration (when present)

Load cells arrive uncalibrated; it is recommended the load cell manufacturer or a qualified technician calibrate these systems on site. Refer to Appendix C for load cell calibration instructions. Expect accuracy of +/- 0.5 kg. Basic load cell default parameters are listed in the electrical schematic included with the ETP.

2.2 Single-Use Bioreactor BPC Loading for 50 - 500 L Volumes

Each outer support container is designed for a specific Single-Use Bioreactor BPC. Confirm the correct volume BPC is being used for the corresponding volume outer support container. The following section outlines the installation and setup of the S.U.B. BPC.

1. Remove irradiated bioreactor BPC from protective double polybags (Figure 2.1).
2. Load S.U.B. BPC from the top into the outer support container (Figure 2.2).
3. Orient S.U.B. BPC with bearing port up and toward motor drive with Kleenpak Connector probe ports facing bottom access cut-out (Figure 2.3).
4. Place the bearing port into bearing port receiver, close door and close clamp (Figure 2.4).
5. Route the side and bottom ports through the side access panel and slot in tank bottom (Figure 2.5, Figure 2.6).
6. Direct the sparges, bottom drain and sampling lines through outer support container access windows (Figure 2.7, Figure 2.8). **NOTE:** The 500 L systems have a hatch covering the access window for the bottom sparge.

Figure 2.1

Figure 2.2

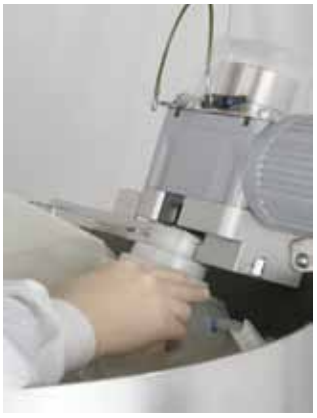


Figure 2.3

Figure 2.4

Figure 2.5

Figure 2.6

Figure 2.7

Figure 2.8

7. Connect incoming gas feed lines to both the overlay filter and the direct sparge filter (Figure 2.9, Figure 2.10).

Figure 2.9

Figure 2.10

8. Inflate S.U.B. BPC with air (inflation time approximately 20 min) through overlay filter, but do not exceed 25 lpm or 0.5 psi (0.34 bar) internal BPC pressure. As BPC inflates, ensure it is properly oriented in the support container (port alignment, drain, sparge, etc.).

WARNING: DO NOT EXCEED 0.5 psi (0.034 bar) within the BPC or BPC could fail. For reference the BPC will appear to be tight at 0.1 psi (0.007 bar). ▲

9. As the bag begins to fill with air, manipulate the bag to align the sparge lines in the base slot (Figure 2.11A, Figure 2.11B).
NOTE: While a sparge line check valve is provided for each sparge line, it is not uncommon for some fluid to bypass check valves during typical use. Elevating the filter to ensure that it is not at the low point of the sparge line will reduce the chance that the filter is exposed to liquid. ▲

Figure 2.11A Membrane Sparge Positioning

Figure 2.11B Aligning Dual Sparge in Base Slot

10. Use the four bottom cut-outs located at the base of the support container as a reference to align hanging tabs on S.U.B. BPC (Figure 2.12).

Figure 2.12

11. Attach platform stretch hooks to each of the four bottom corners of the BPC (Figure 2.13).

Figure 2.13

12. Position bottom-side drain, pulling out/downward to position port towards bottom edge of tank.
13. Align row of Kleenpak Connector probe ports within access window (Figure 2.14).

Figure 2.14

NOTE: Verify all port clamps are closed and located as CLOSE as possible to the body of the S.U.B. BPC. ▲

NOTE: Air fill of the S.U.B. BPC takes approximately 10-20 minutes to allow for drive shaft insertion (times will vary based on flow rate, inlet pressure and bag volume). The BPC must be at least partially inflated in order to insert drive shaft. ▲

14. Remove the latch pin from the safety cover over the mixing assembly and open the cover. Unscrew the threaded cap covering the hollow pass-through of the motor (Figure 2.15).

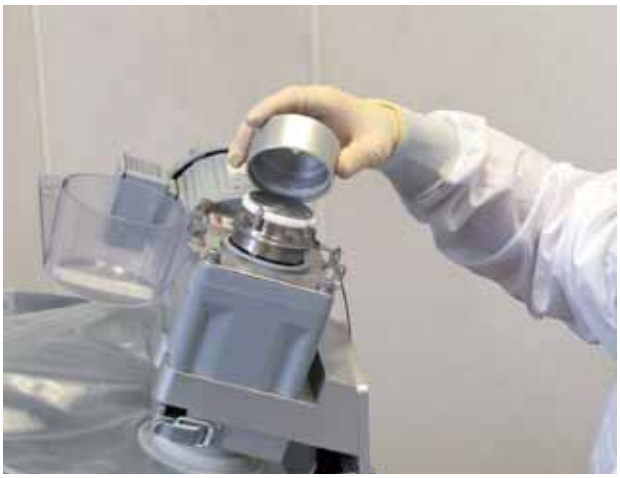


Figure 2.15. Mixing Assembly

15. Split shaft assembly–500 L system only: Verify the two sections of the drive shaft are located in the drive shaft holders near the side of the outer support container. The sections will be referred to as upper (section with the drive shaft head), and lower (section with the square end). Lubricate the threaded ends with a light coat of food grade anti-seize with each use.
    - Insert lower section of drive shaft through hollow pass-through of mixing assembly (Figure 2.16).
    - Once inserted, slide latch pin from mixing assembly into shaft to prevent it from falling into the tube (Figure 2.17).
    - Assemble the upper and lower sections of the drive shaft by joining the segments and with a counterclockwise motion, hand tighten the two sections together (Figure 2.18). Remove latch pin.
    - Locate one wrench on the flat area in the lower drive shaft section, another wrench on the upper section and tighten the connection using a counterclockwise rotation (Figure 2.19). The shafts are reverse threaded to avoid loosening during operation. **CAUTION:** Do not over tighten; a snug fit is sufficient.

- Once the sections are secure, return the wrenches to the tool holder.

Figure 2.16

Figure 2.17

Figure 2.18

Figure 2.19

Drive Shaft Insertion (50- 500L Volumes)

16. Insert drive shaft through hollow pass-through of mixing assembly in the following manner (Figures 2.20 - 2.23).
    - Use two hands to load drive shaft through top of mixing assembly; a slight back and forth twisting motion will aid in insertion and avoid stretching of the impeller tubing.
    - When approximately 2-3" (5.08 cm) of shaft remains, twist slightly to engage impeller.
    - When approximately 1-2" (2.54 cm) of shaft remains, twist slightly to engage bearing assembly.
    - When approximately 0.25" (0.64 cm) of shaft remains, twist to align motor drive keyway with one of the four outer slots on the drive shaft head.

Figure 2.20

Figure 2.21

Figure 2.22

Figure 2.23

17. Directly couple drive shaft to motor drive (Figures 2.24 - 2.26).
    - Place threaded cap on hollow pass-through and hand tighten clockwise.
    - Tighten cap by placing spanner wrench on hollow pass-through and tighten cap using supplied torque wrench.
      NOTE: The torque wrench is a standard 3/8" square drive, and it is calibrated at the factory at 150 in-lbs.
    - Verify wrenches have been removed from system and placed in storage holders.
    - Close safety access cover and insert latch pin.

Figure 2.24

Figure 2.25

Figure 2.26

18. The air supply to the overlay can be turned off once the drive shaft has been inserted.

Final Installation Steps

19. Optional: Wrap and secure vent filter heater on exhaust filter. Connect heater to controller and verify it is plugged into an appropriate 120 or 240 VAC outlet, then connect the power cord to the controller. **NOTE:** Controller is preset to 50°C.
20. Secure exhaust vent filter on side-mounted holder (Figure 2.27A and 2.27B). **NOTE:** 500 L S.U.B. bags and some custom S.U.B. BPCs are supplied with dual exhaust vents. Extended single and dual exhaust vent brackets are available (see section 4.3 for ordering information).

Figure 2.27A

Figure 2.27B

21. Position and close a bar clamp (Part No. SV20664.01) on the bottom drain line as close as possible to the BPC port (Figure 2.28).

Figure 2.28

22. Insert RTD or selected temperature sensor into thermo-well (Figure 2.29, Figure 2.30).
    a. Place small amount of glycerol (0.5 mL) in well to aid in heat transfer.
    b. Sensor should be inserted until base of probe meets the mouth of the thermo-well.
    c. Secure by twisting the luer lock collar if provided. The thermo-well will stretch slightly when RTD is seated.

Figure 2.29

Figure 2.30

23. Optional: Connect pressure transducer to user-supplied monitoring device.
24. Continue to Section 2.5 for probe insertion instructions.
25. Close the bottom access hatch (500 L only). The proper latch tension can be obtained by a combination of feel and visual inspection. When closing the latch the handle should begin to provide resistance to closing when the leading edge of the safety pin pass through of the latch handle aligns with the outside edge of the latch base (Figure 2.31). **NOTE:** When the latch is under-tensioned the safety pin pass through of the latch handle will be covered within the latch base and the handle will close very easily. If the latch is over-tensioned the handle will be excessively difficult to close.
26. The access doors must be closed and fully latched prior to filling the system with liquid.

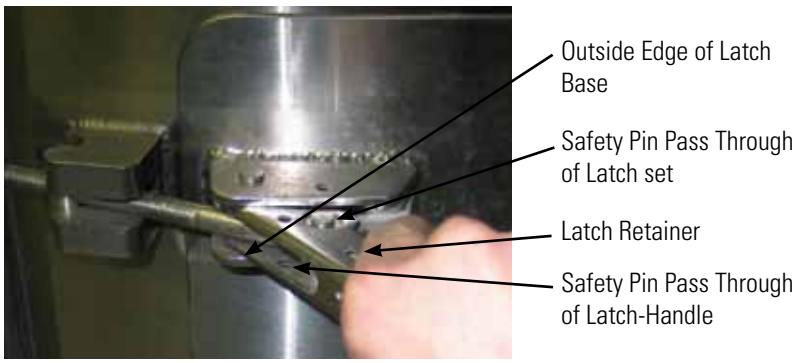


Figure 2.31

2.3 Single-Use Bioreactor BPC Loading for 1000 L Electric Resistive Heater

Before beginning, verify that the outer support container is stationary with casters locked into place. BPC loading may require operators to step inside the bioreactor and the unit must be stationary for the safety of both operator and equipment. For ease in BPC loading, two operators may be required. For drive shaft insertion, a ladder or other means of elevation is required.

1. Open both doors on bioreactor support container and reach inside to open clamp on bearing port receiver located below the motor (Figure 2.32, Figure 2.33). If attached, remove the probe shelf from the front of the tank cut-out and store on the platform.

Figure 2.32

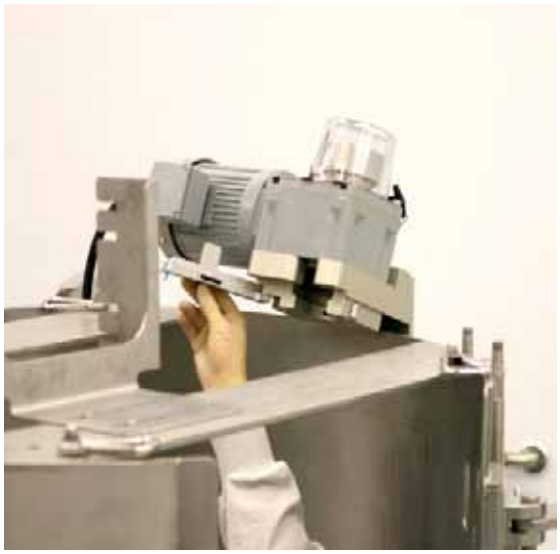


Figure 2.33

2. Remove irradiated S.U.B. BPC from protective double polybags (Figure 2.34). Do not remove the polybags from the line sets at this stage as the BPC may become difficult to manage. Do not allow the BPC or line sets to touch or drag on the floor.

Figure 2.34

3. Reach into or step inside the outer support container with the front face (bearing port side) of the BPC oriented towards the motor (Figure 2.35).

Figure 2.35

4. Place the top line sets (still in polybags) on top of the cross supports located on the top of the outer support container (Figure 2.36). This will keep the BPC from being restricted during the air inflation step.

Figure 2.36

5. Load the BPC bearing port into the receiver (Figure 2.37) and close the door and clamp (Figure 2.38).

Figure 2.37

Figure 2.38

6. Remove the bubble wrap from the sparge filters. Guide the sparge inlet lines and filters through the bottom cutouts in the outer support container (Figure 2.39); the operator can reach just below the tank to further extend the sparge lines from the cutouts (Figure 2.40).

Figure 2.39

Figure 2.40

Pass the bagged drain line set and temperature/sampling port set through the large cut-out in the front of the outer support container (Figure 2.41). Extend the drain line set through the cut-out (Figure 2.42).

Figure 2.41

Figure 2.42

Gas Supply Connections and Air Inflation

The BPC should be partially inflated to allow for proper insertion of the drive shaft and to aid in proper alignment of the BPC in the outer support container.

8. Connect pressure transducer to monitor and once the display has stabilized, tare the monitor (the monitor should be allowed to warm up for 30 minutes before taring). Verify that the monitor reads zero.
9. Attach air supply to overlay gas inlet line.

NOTE: Air pressure to the overlay gas line on the S.U.B. BPC should not exceed 3 psi (less than 25 lpm). ▲

WARNING: DO NOT EXCEED 0.5 psi (0.34 bar) within the BPC or the system could fail causing personal injury or damage to equipment. **DO NOT leave the BPC unattended while inflating.** ▲

10. Begin air inflation through the overlay gas line.
11. While the BPC is inflating, attach the incoming gas supply to the sparger gas inlet line.

NOTE: Air pressure to the sparger on the S.U.B. BPC should not exceed 8 psi. Also, while a sparge line check valve is provided for each sparge line, it is not uncommon for some fluid to bypass check valves during typical use. Elevating the filter to ensure that it is not at the low point of the sparge line will reduce the chance that the filter is exposed to liquid. ▲

12. Tare the load cell display before proceeding.
13. Using the four stretch hooks provided, secure the BPC by attaching the hooks to the hanging tabs on the bottom of the BPC (Figure 2.43, Figure 2.44). Verify that the sparge filter and sparge remain in position while attaching the stretch hooks. It is recommended that users secure the hanging tabs on the front BPC panel first. This way the door will not be an obstruction when connecting the last set of stretch hooks.

Figure 2.43

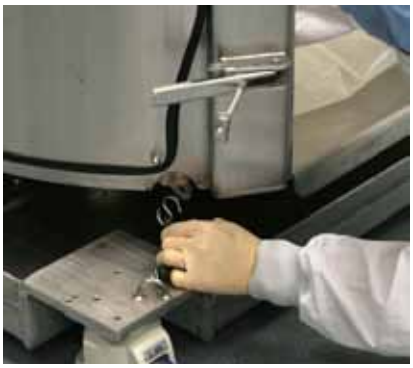


Figure 2.44

14. While BPC begins to fill with air, remove the protective packaging from the exhaust vent filters (Figure 2.45).

Figure 2.45

15. Air fill of the S.U.B. BPC takes approximately 15-20 minutes before drive shaft insertion can begin (times will vary based upon flow rate and inlet pressure) (Figure 2.46).

Figure 2.46

Four hanging tab hooks are located on the top of the outer support container. These hooks can be used to secure the BPC from the top hanging tabs once it is inflated.

Drive Shaft Insertion

The drive shaft is constructed in three or four pieces which must be assembled and inserted piecewise. Reminder: Operators should be elevated (i.e. ladder) to effectively assemble and insert the drive shaft.

16. Prepare the hollow pass-through by first removing the latch pin on the safety cover (Figure 2.47), opening the safety cover (Figure 2.48) and removing the threaded cap (turn counterclockwise) of the mixing assembly (Figures 2.49 and 2.50).

Figure 2.47

Figure 2.48

Figure 2.49

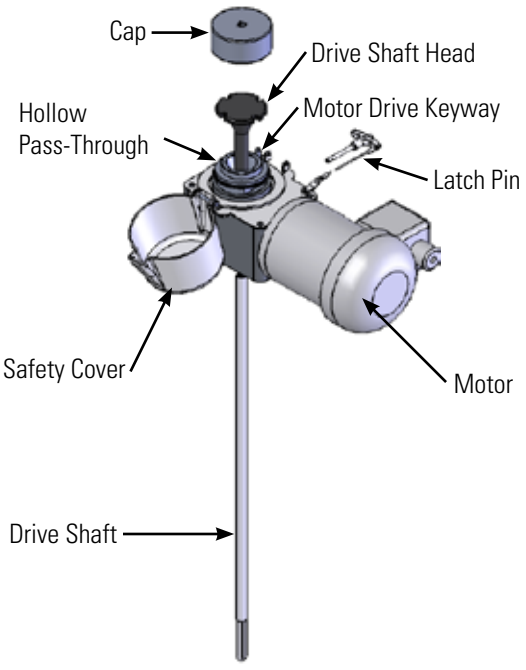


Figure 2.50. Mixing Assembly

17. Verify the three sections of the drive shaft are located in the drive shaft holders on the side of the outer support container. The sections will be referred to as the upper (section with the drive shaft head), middle (section with internal/external threads on each end) and lower (section with the square end). Lubricate the threaded ends with a light coat of food grade anti-seize with each use.
18. First insert the lower section through the hollow pass-through of the mixer drive (Figure 2.51). Slide latch pin from mixing assembly into shaft to prevent it from falling into the tube. Assemble the middle and lower sections of the drive shaft by joining the segments with a twisting motion, fasten the two sections together (Figure 2.52). **NOTE:** Segmented shaft threads are left handed. Locate one wrench on the flat area in the middle drive shaft section, another wrench on the lower section and tighten the connection using a counterclockwise rotation (Figure 2.53). The shafts are reverse threaded to avoid loosening during operation. Once the sections are secure, return the wrenches to the tool holder. **CAUTION:** Do not over tighten; a snug fit is sufficient. Remove the latch pin.

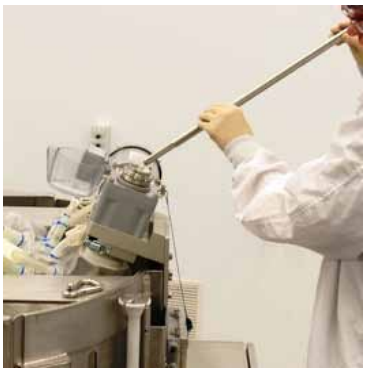


Figure 2.51

Figure 2.52

Figure 2.53

Load the partially assembled drive shaft through the hollow pass-through and hold it in position sufficient to allow a wrench to be placed on the upper most flats of this shaft section. Obtain the upper section of the drive shaft and assemble it to the other segment in the manner described previously (Figure 2.54, Figure 2.55).

Figure 2.54

Figure 2.55

19. Using two hands, carefully guide the completed drive shaft into the BPC using a slight back and forth twisting motion (Figure 2.56).
    NOTE: It may be necessary for another operator to assist with drive shaft insertion. As one operator inserts the drive shaft, another operator should carefully manipulate the impeller when the end of the drive shaft begins to couple with the impeller.
    a. When 2-3” (5.08 cm) of shaft remains, twist slightly to engage the impeller.
    b. When 1-2” (2.54 cm) of shaft remains, twist slightly to engage bearing assembly.
    c. When 0.25-.50” (0.64 cm) of shaft remains, twist to align motor drive keyway with one of the four outer slots on the drive shaft head.

Figure 2.56

20. Directly couple the drive shaft to the motor by placing the threaded cap back on the hollow pass-through and tighten.
21. Tighten cap by placing spanner wrench counterclockwise on hollow pass-through and tighten using supplied torque wrench (Figure 2.57). **NOTE:** The torque wrench is a standard 3/8" square drive and it is calibrated at the factory at 150 in-lbs.

Figure 2.57

22. Verify wrenches have been removed from the system and returned to the storage holders.
23. Close safety access cover and insert latch pin.

Securing Access Doors (Resistive Heater Only)

The procedures listed below must be followed in full detail and in proper order to ensure the S.U.B. outer support container is operated in a safe manner. The outer support container is subjected to high structural loads due to the weight and pressure of the fluid and gas contained in the BPC. In order to ensure structural integrity of the system it is necessary for the tension on each door be even and involves a two step tensioning procedure of the latches. Neglecting these instructions may result in personal injury and/or permanent damage to hardware system. The access doors of the outer support container should never be opened when the BPC is filled with liquid.

24. Close both the left and right side access doors of the outer support container while paying close attention to ensure the BPC is not pinched in any of the door seams.

25. Each door is supplied with four side latches; the closure sequence and tension method must be performed in the following manner (Figure 2.58). Following this sequence will ensure that the outer support container will retain the proper shape and structure after repeated use.

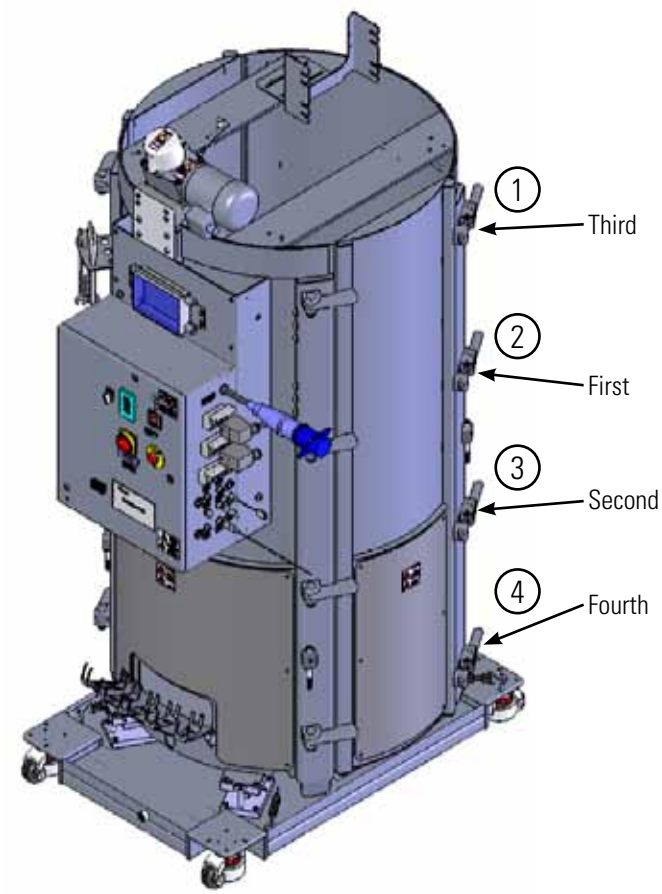


Figure 2.58. Latch Closure Sequences (latch references are shown in circles)

26. The doors should be secured first with the two middle latches (latches 2 and 3). Proper tension is obtained by adjusting the threaded latch pin. Tension of the latch is adjusted by varying the position of the pin on the threaded shank (Figure 2.59).

Figure 2.59

27. The proper latch tension can be obtained by a combination of feel and visual inspection. When closing the latch the handle should begin to provide resistance to closing when the leading edge of the safety pin pass through of the latch handle aligns with the outside edge of the latch base (Figure 2.60). **NOTE:** When the latch is under-tensioned the safety pin pass through of the latch handle will be covered within the latch base and the handle will close very easily. If the latch is over-tensioned the handle will be excessively difficult to close.

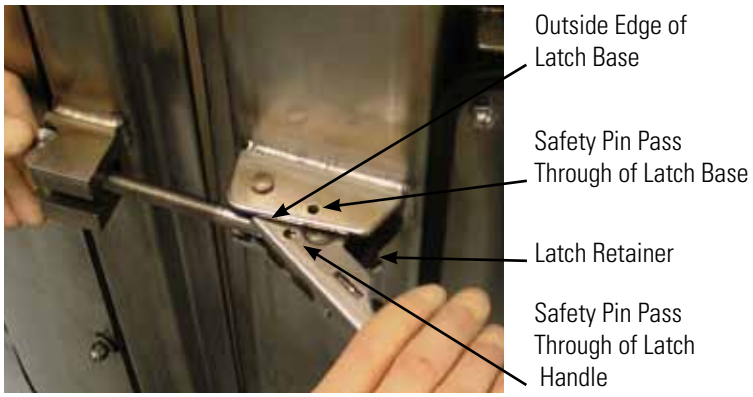


Figure 2.60

28. Once the two middle latches are closed, the top (latch 1) and bottom latches (latch 4) can be closed using the same tensioning procedures.
29. Both the left and right access doors must be closed and fully latched prior to proceeding to the final latch tensioning procedures. The final procedure that follows must be performed one latch at a time.
30. Release latch 2 (notice that tension on the latch is less than seen when the latch was first closed) and adjust the threaded latch pin sufficient to allow the latch handle to begin to tension.
31. Release latch 3 and adjust the tension as in the previous step.
32. Release latch 1 and adjust the tension and close.
33. Release latch 4 and adjust the tension and close.
34. For maximum security insert safety pins (not included) into the respective latches.
35. Once the drive shaft is inserted and side access doors closed, turn off the air supply to the overlay line. If the optional exhaust vent filter heaters are being used, secure heaters to the filter at this time.

Final Installation Steps

Secure exhaust vent filters on top-mounted holders by use of the filter side vents (Figure 2.61A) or if using elevated dual exhaust filters, use the adapter piece and extended filter bracket (Figure 2.61B).

Figure 2.61A

Figure 2.61B Extended Dual Filter Bracket

37. Fully extend the drain line set through the front cutout and attach the probe shelf.
38. Remove the poly bag from the drain line set and position the line clamp as close as possible to the BPC port and close. Use a cable tie around the clamp to ensure the clamp cannot be accidentally opened.
39. Align the five Kleenpak ports through the front access window (Figure 2.62).

Figure 2.62

40. Insert RTD or selected temperature sensor into the thermo-well (Figure 2.63).
    a. Place a small amount of glycerol (0.5 mL) in well to aid in heat transfer.
    b. Sensor should be inserted until base of RTD meets the mouth of the thermo-well.
    c. Secure by twisting the luer lock collar if provided the thermo-well will stretch slightly when RTD is seated (Figure 2.64).

Figure 2.63

Figure 2.64

NOTE: Verify all port clamps are closed and located as near as possible to the body of the S.U.B. BPC**.** ▲

Loading 1000 L Water Jacket

1. Open both the upper and lower doors on outer support container and reach inside to open clamp on bearing port receiver located below the motor (Figure 2.65). If attached, remove the probe shelf from the front of the tank cut-out and store on the platform.
2. Remove irradiated S.U.B. BPC from protective double polybags. Do not remove the polybags from the line sets at this stage as the BPC may become difficult to manage. Do not allow the BPC or line sets to touch or drag on the floor.
3. Load the BPC through the top access door; orient the bottom of the BPC first with the bearing port facing upward (Figure 2.66).

Figure 2.65

Figure 2.66

4. Place the top line sets (still in polybags) over the side of the outer support container. This will help support the weight of the BPC and also keep the BPC from being restricted during the air inflation step.
5. Load the BPC bearing port into the receiver (Figure 2.67) and close the door and clamp (Figure 2.68).

Figure 2.67

Figure 2.68

6. Connect pressure transducer to monitor. Once the display has stabilized, tare the monitor (the monitor should be allowed to warm up for 30 minutes before taring). Verify that the monitor reads zero.

Gas Supply Connections and Air Inflation

The BPC should be partially inflated in order to aid in proper alignment of the BPC in the outer support container and will be necessary to allow for proper insertion of the drive shaft.

7. Attach air supply to overlay gas inlet line at the top of the BPC.

NOTE: Air pressure to the overlay gas line on the S.U.B. BPC should not exceed 3 psi (less than 25 lpm). ▲

WARNING: DO NOT EXCEED 0.5 psi (0.34 bar) within the BPC or the system could fail, causing personal injury or damage to equipment. DO NOT leave the BPC unattended while inflating. ▲

NOTE: Air pressure to the sparger on the S.U.B. BPC should not exceed 8 psi. Also, while a sparge line check valve is provided for each sparge line, it is not uncommon for some fluid to bypass check valves during typical use. Elevating the filter to ensure that it is not at the low point of the sparge line will reduce the chance that the filter is exposed to liquid. ▲

8. Remove the bubble wrap from the bottom sparge filter. Use the lower door to gain access to floor of the hardware, guide the sparge inlet line and filter through the bottom cutout in the outer support container (Figure 2.69). Two holes are present in the tank; the hole furthest from tank centerline should be utilized with standard S.U.B. BPC having a single sparge port (a supplied cover plate is typically used to cover the second hole when using a standard BPC). The operator can reach just below the tank to further extend the sparge line from the cut-out (Figure 2.70).

Figure 2.69

Figure 2.70

9. By use of the access door, pass the bagged drain line set and temperature/sampling port set through the large cutout in the front of the outer support container (Figure 2.71). Extend the drain line set through the cutout.

Figure 2.71

10. Tare the load cell display before proceeding.
11. Using the four stretch hooks provided, secure the BPC by attaching the hooks to the hanging tabs on the bottom of the BPC (Figure 2.72). Verify that the sparge filter and sparge remain in position while attaching the stretch hooks. It is recommended that users secure the hanging tabs on the front BPC panel first. This way the door will allow access when connecting the last set of stretch hooks.

Figure 2.72

12. While BPC begins to fill with air, remove the protective packaging from the exhaust vent filters. If the bag is filled sufficiently with air the filters can be loaded into the holder (Figure 2.73A). If using elevated exhaust vent filters, use the corresponding extended dual vent filter bracket (Figure 2.73B).
13. Four hanging tab hooks are located on the top of the outer support container. These hooks can be used to secure the BPC from the top hanging tabs once it is inflated. If connecting all four corners requires excessive stretching of the BPC it is acceptable to only use two or more hooks (preferably at opposite corners)(Figure 2.74).

Figure 2.73A

Figure 2.73B

Figure 2.74

Drive Shaft Insertion

The drive shaft is constructed by assembling three or four pieces; these must be assembled and inserted piecewise in areas having low ceilings. Reminder: Operators should be elevated (i.e. ladder) to effectively assemble and insert the drive shaft.

14. Verify the drive shaft sections and tools are available.
15. Prepare the hollow pass-through by first removing the latch pin on the safety cover (Figure 2.75), opening the safety cover and removing the threaded cap [turn counterclockwise] (Figure 2.76) of the mixing assembly (Figures 2.77).

Figure 2.75

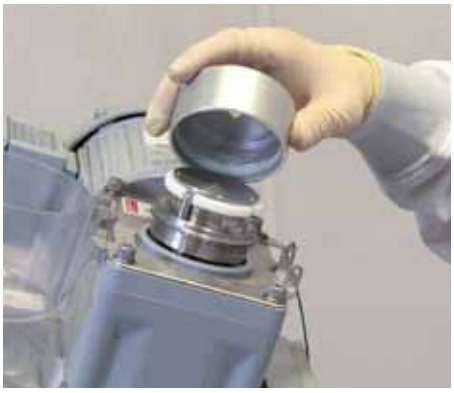


Figure 2.76

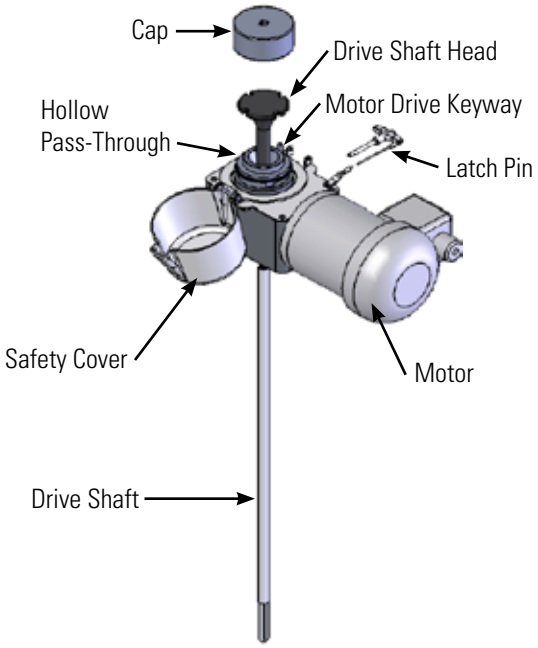


Figure 2.77 Mixing Assembly

16. Verify the three sections of the drive shaft are located in the drive shaft holders on the side of the outer support container. The sections will be referred to as the upper (section with the drive shaft head), middle (section with internal/external threads on each end) and lower (section with the square end). Lubricate the threaded ends with a light coat of food grade anti-seize with each use.
17. First insert the lower section through the hollow pass-through of the mixer drive (Figure 2.78). Once inserted, slide latch pin from mixing assembly into shaft to prevent it from falling into the tube (Figure 2.79). Assemble the middle and lower sections of the drive shaft by joining the segments and with a twisting motion, fasten the two sections together (Figure 2.80). **NOTE:** Segmented shaft threads are left handed. Locate one wrench on the flat area in the middle drive shaft section, another wrench on the lower section, and tighten the connection using a counterclockwise rotation (Figure 2.81). The shafts are reverse threaded to avoid loosening during operation. **CAUTION**: Do not over tighten; a snug fit is sufficient. Remove the latch pin.

Figure 2.78

Figure 2.79

Figure 2.80

Figure 2.81

Remove the latch pin, load the partially assembled drive shaft through the hollow pass-through and hold it in position sufficient to allow the latch pin to be inserting in to the next set of holes and allow the wrench to

be placed on the upper most flats of this shaft section. Obtain the upper section of the drive shaft and assemble it to the other segment in the manner described previously (Figure 2.82, Figure 2.83). Once the sections are secure remove the latch pin and return to the wrenches to the tool holder.

Figure 2.82

Figure 2.83

19. Using two hands, carefully guide the completed drive shaft into the BPC using a slight back and forth twisting motion or a counter-clockwise rotation.
    - When 2-3" (5.08 cm) of shaft remains, twist slightly to engage the impeller.
    - When 1-2" (2.54 cm) of shaft remains, twist slightly to engage bearing assembly (Figure 2.84).
    - When ~0.25" (0.64 cm) of shaft remains, twist to align motor drive keyway with one of the four outer slots on the drive shaft head.
20. Ensure the head is fully seated before directly coupling the drive shaft to the motor by placing the threaded cap back on the hollow pass-through and tightening it.
    NOTE: The cap should be easy to install when the drive shaft head is fully engaged in the hollow pass-through. Otherwise repeat all steps of #19 before installing cap.

Figure 2.84

21. Directly couple the drive shaft to the motor by placing the threaded cap back on the hollow pass-through and tighten.
22. Tighten cap by placing spanner wrench (counterclockwise) on hollow pass-through and tighten using supplied torque wrench (Figure 2.85). **NOTE:** The torque wrench is a standard 3/8" square drive and it is calibrated at the factory at 150 in-lbs.

Figure 2.85

Securing Access Doors

23. Verify wrenches have been removed from the system and returned to the storage holders.
24. Close safety access cover and insert latch pin.
25. The access doors should be secured first with the latches. Proper tension is obtained by adjusting the threaded latch pin. Tension of the latch is adjusted by varying the position of the pin on the threaded shank.
26. The proper latch tension can be obtained by a combination of feel and visual inspection. When closing the latch the handle should begin to provide resistance to closing when the leading edge of the safety pin pass through of the latch handle aligns with the outside edge of the latch base. (Figure 2.86) **NOTE:** When the latch is under-tensioned the safety pin pass through of the latch handle will be covered within the latch base and the handle will close very easily. If the latch is over-tensioned the handle will be excessively difficult to close.

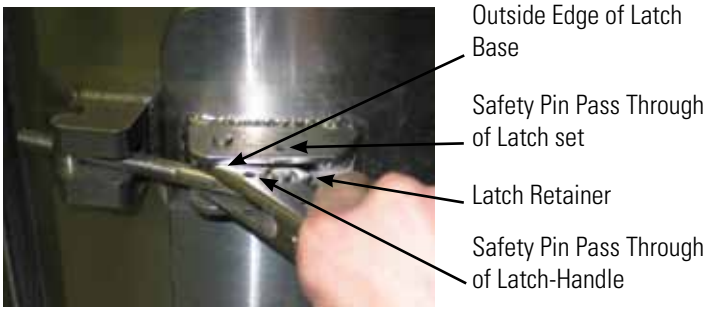


Figure 2.86

Final Installation Steps

27. For maximum security insert safety pins (not included) into the respective latches.
28. Once the drive shaft is inserted and side access doors closed, turn off the air supply to the overlay line. If the optional exhaust vent filter heaters are being used, secure heaters to the filter at this time.
29. Verify position of the exhaust vent filters on top-mounted holders by use of the velcro fasteners (Figure 2.87).

Figure 2.87

30. Fully extend the drain line set through the front cutout and attach the probe shelf.
31. Remove the poly bag from the drain line set and position the line clamp as close as possible to the BPC port and close. Use a cable tie around the clamp to ensure the clamp cannot be accidentally opened.
32. Align the five Kleenpak ports through the front access window (Figure 2.88). This will be the lower cutout if hardware is supplied with two horizontal slots.

Figure 2.88

33. Insert RTD or selected temperature sensor into the thermo-well (Figure 2.89).
    a. Place a small amount of glycerol (0.5 mL) in well to aid in heat transfer (Glycerol - Sigma G6279).
    b. Sensor should be inserted until base of RTD meets the mouth of the thermo-well.
    c. Secure by twisting the luer lock collar if provided. The thermo-well will stretch slightly when RTD is seated (Figure 2.90).

Figure 2.89

Figure 2.90

NOTE: Verify all port clamps are closed and located as near as possible to the body of the S.U.B. BPC**.** ▲

2.4 Loading 2000 L Water Jacket

1. Main power to the control panel should be switched on. Ensure that the drive motor is not running. Open both the front and rear doors on outer support container and use an elevated platform to open clamp on bearing port receiver located below the motor (Figure 2.91). Lower the hoist lifting frame to a position just above the top of the rear door by using the pneumatic control lever near the rear door.

2. Two operators should carefully remove irradiated S.U.B. BPC from protective double polybags. Do not remove the polybags from the line sets at this stage as the BPC may become difficult to manage. Do not allow the BPC or line sets to touch or drag on the floor.

3. Load the BPC through the rear access door; orient the bottom of the BPC into the door first with the bearing port facing upward (Figure 2.92). Keep the BPC folded as supplied in the packaging, it will allow the bag to unfold naturally when lifted by the hoist.

Figure 2.91

Figure 2.92

4. Using the rear door for access, connect the retainer hooks of the hoist to the top of the BPC via the hanging tabs starting with the furthermost two tabs (Figure 2.93) and finishing with the closer two tabs (Figure 2.94).

5. Raise the BPC using the pneumatic lift, one operator observing from above with the second operator at ground level controlling the lifting valve (Figure 2.95).

6. Raise the hoist until the lift reaches full stroke. Once lifting stops the top level operator should hold the hoist frame and apply some minimal lifting force. This will assist the lifting device to pull in any remaining slack in the cable and ensure the lift device has been fully raised. Place the valve in the stop position.

Figure 2.93

Figure 2.94

Figure 2.95

7. Place the top line sets (still in polybags) onto the lifting frame or over the side of the outer support container. This will help support the weight of the BPC and also keep the BPC from being restricted during the air inflation step.

8. Remove the black protective cap from the bearing port (Figure 2.96), load the BPC bearing port into the receiver (Figure 2.97) and close the bearing assembly door and clamp (Figure 2.98).

Figure 2.96

Figure 2.97

Figure 2.98

9. Open the tubing set polybag and connect pressure transducer to monitor. Once the display has stabilized, tare the monitor (the monitor should be allowed to warm up for 30 minutes and the sensor connected for 10 minutes before taring). Verify that the monitor

Gas Supply Connections and Air Inflation

reads zero.

The BPC must be partially inflated in order to aid in proper alignment of the BPC in the outer support container and is necessary to allow for proper insertion of the drive shaft.

10. Attach air supply to overlay gas inlet line at the top of the BPC. Operators should allow the bag to fill to greater than half volume (typically > 20 minutes).

    NOTE: Air pressure to the overlay gas line on the S.U.B. BPC should not exceed 5 psi (less than 100 lpm). ▲

    WARNING: DO NOT EXCEED 0.5 psi (0.34 bar) within the BPC or the system could fail, causing personal injury or damage to equipment. DO NOT leave the BPC unattended while inflating. ▲

11. Feed the probe belt, sample line, and the subsurface addition lines through the front access door (Figure 2.99)

12. Remove sparge lines from the poly bags and bubble wrap from sparge filters. Use the rear door to gain inside access to the floor of the hardware. Place a clamp on the bottom drain line at this time (Figure 2.100).

Figure 2.97

Figure 2.98

13. Guide the sparge inlet line and filter through the bottom cutout in the outer support container.
    - The plastic center tank insert of the floor provides the port locations for both the bottom drain (Figure 2.101) and the open pipe sparge (Figure 2.102).
    - Opening the pivoting access cover in the bottom of the tank will allow access for loading the frit sparge gas line (Figure 2.103).

Figure 2.101

Figure 2.102

Figure 2.103

Figure 2.104

Three cut-out holes are provided in the tank for frit sparges; these holes are furthest from tank center line and align with the inside edge of this access cover door (Figure 2.104).

NOTE: Air pressure to the sparger on the S.U.B. BPC should not exceed 8 psi. Also, while a sparge line check valve is provided for each sparge line, it is not uncommon for some fluid to bypass check valves during typical use. We recommend elevating the sparge line filter as is feasible to help reduce this tendency. ▲

14. Tare the load cell display before proceeding.

15. Using the positioning tab pins provided, secure the BPC by attaching the tabs on the bottom of the BPC onto the position tab pins (Figure 2.105, 2.106). Verify that the sparge filter and sparges remain in position while attaching the tabs. It is recommended that users secure the tabs on the front BPC panel first. This way the larger rear door will allow access when connecting the last set of tab pins.

Figure 2.105

Figure 2.106

16. While the BPC begins to fill with air, remove the protective packaging from the exhaust (vent) filters. If the bag is filled sufficiently with air the filters can be loaded into the holder.
    - If using the exhaust condenser system, follow the setup instructions in Section 2.4.
    - If using elevated exhaust vent filters, use the corresponding extended dual vent filter bracket and filter heaters. Follow the setup instructions in Section 2.4.

Disposable Exhaust Condenser

Condenser System Functional Overview

The condenser system is intended to be used as an accessory to the Single-Use Bioreactor (S.U.B.) as an alternative to vent filter heaters. The condenser's purpose is to prevent liquids and solids from condensing and collecting inside of the vent filters of the S.U.B. The condenser system cools the exhaust gasses leaving the S.U.B. chamber, condensing the moisture out of the saturated gasses coming from the S.U.B. The liquid condensate that is stripped from the exhaust gasses is then pumped back into the S.U.B. chamber, creating a sterile loop and significantly reducing liquid loss due to evaporation. The condenser plate is chilled by a closed bath recirculating chiller which has sufficient capacity to cool two condenser plates simultaneously. Figure 2.107 shows a functional diagram of the condenser system.

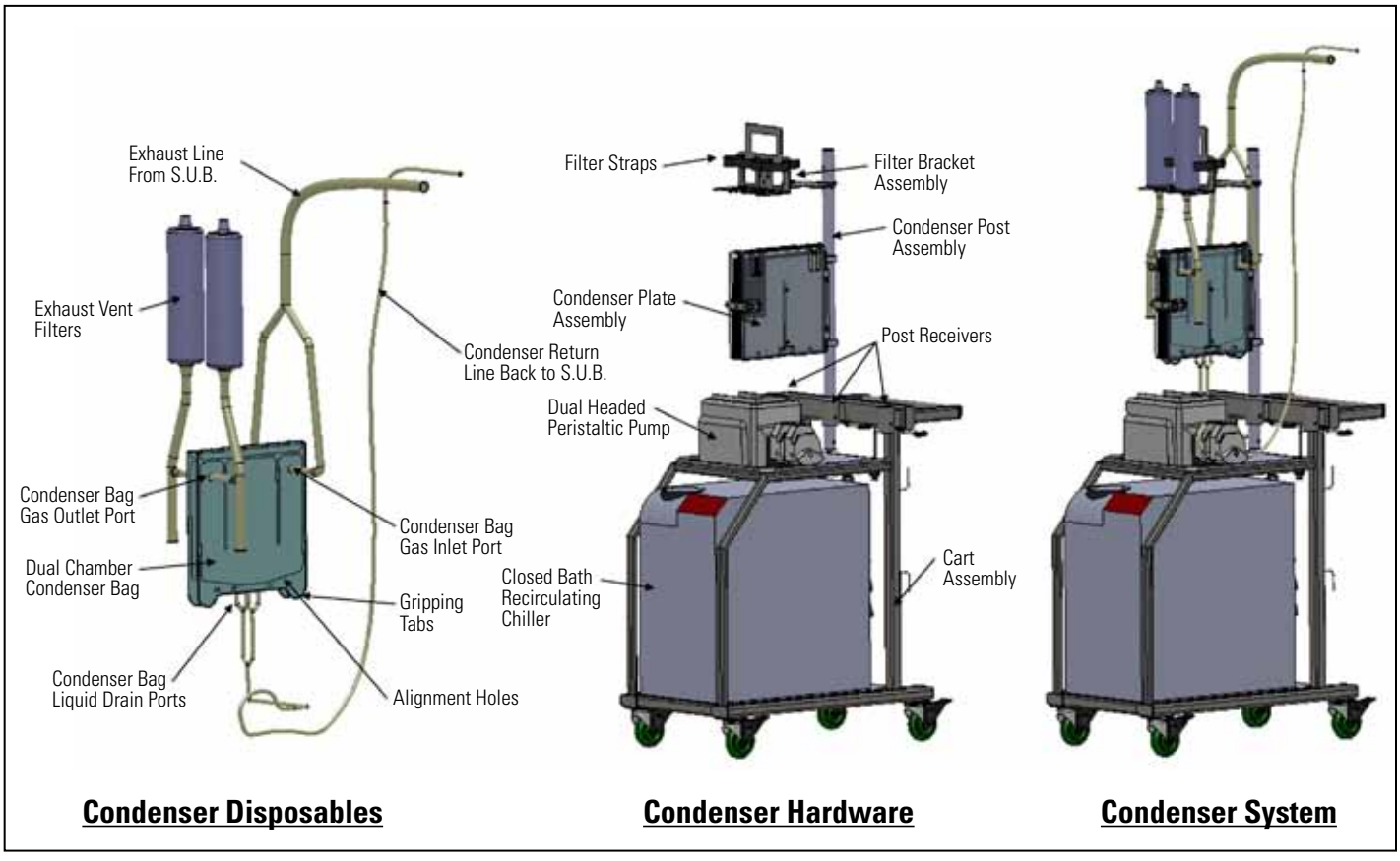


Figure 2.107. Condenser System Overview

Guidance for when to use the Condenser System

2000 L S.U.B.–BPC with Single-Use Condenser System

Large 10” hydrophobic PVDF filters with a nominal 0.2 micron pore size were specified in order to increase the available surface area for off-gassing. In conjunction, the standard 2000 L S.U.B. is designed for use with a single use condenser system. This allows the S.U.B. to utilize a powerful phase-change type system which provides improved exhaust vent protection and reliability due to the ability to strip condensate and atomized materials that may be present from the off-gas stream of the S.U.B. This system has been shown to significantly reduce the “fouling” load on the vent filters that inherently increases operating back pressure as the cell culture run batch progresses. See Single-Use Bioreactor Validation Guide for specific details.

2000 L S.U.B.–BPC with Vent and Heaters Only

Some end-users may prefer to omit the Condenser System on the 2000 L S.U.B. under the expectation that this will allow for a more uniform installation (similar to smaller S.U.B.s used in the upstream seed train), or will perhaps reduce system complexity and cost. The use of exhaust vent heaters and 10” filters will provide some impressive flow capacity over short periods (<5-days). However, the high sparge rates required during the scale-up of the S.U.B. to the 2000 L working volume may eventually create conditions of increased operating back pressure, usually due in part to blocking of the filter media. Depending upon the application, the user has the option of using both filters in parallel or initiating the run with a single filter, temporarily clamping off the line to the other filter (it being reserved as redundant back-up).

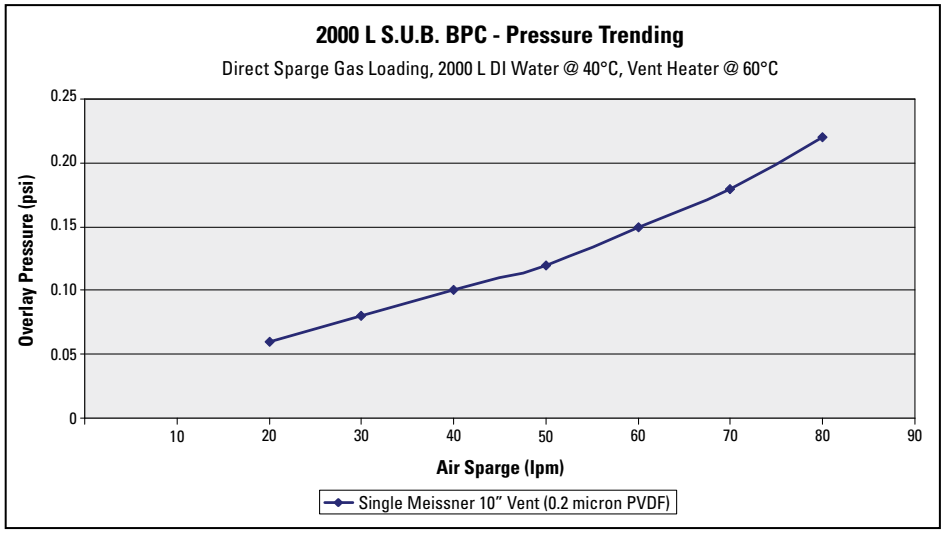
NOTE: The disposable Condenser System has the potential to provide continuous and nearly indefinite protection against performance degradation of the exhaust vent filters (rated for continuous flow rates up to a total off-gassing rate of 50 lpm and intermittent flows up to 100 lpm). See Single-Use Bioreactor System Validation Guide.

Table 2.1 can help end-users specify the BPC configuration and operating parameter setup for custom 2000 L S.U.B. applications when not utilizing the disposable exhaust condenser. Because the operating parameters of different cell cultures vary widely, a safety factor should be used to temper the data. As such, the data we used to generate a control base line are for reference only (filter fouling will vary and must be considered to ensure reliable performance). It is assumed no foam is present in the exhaust stream.

S.U.B. System (2 ea 10" vents)	Run Duration	Max. Combined Flow Rate Recommended	Resulting Safety Factor
2000 L S.U.B.	7 days	40 lpm	2X
2000 L S.U.B.	10 days	32 lpm	2.5X
2000 L S.U.B.	14 days	27 lpm	3X
2000 L S.U.B.	21 days	Strongly Recommend: Single Use Condenser	

Table 2.1. Condenser System Overview

The above recommendations were generated using the test conditions shown in Graph 2.1. In this case a 2000 L S.U.B. was filled with 2000 L of DI water with a batch temperature of 40°C using a MKS vent filter heater at 60°C. Safety factor estimates are based on a maximum continuous internal S.U.B. BPC pressure not to exceed 0.1 psi (which corresponds to 40 lpm with a single 10" vent).

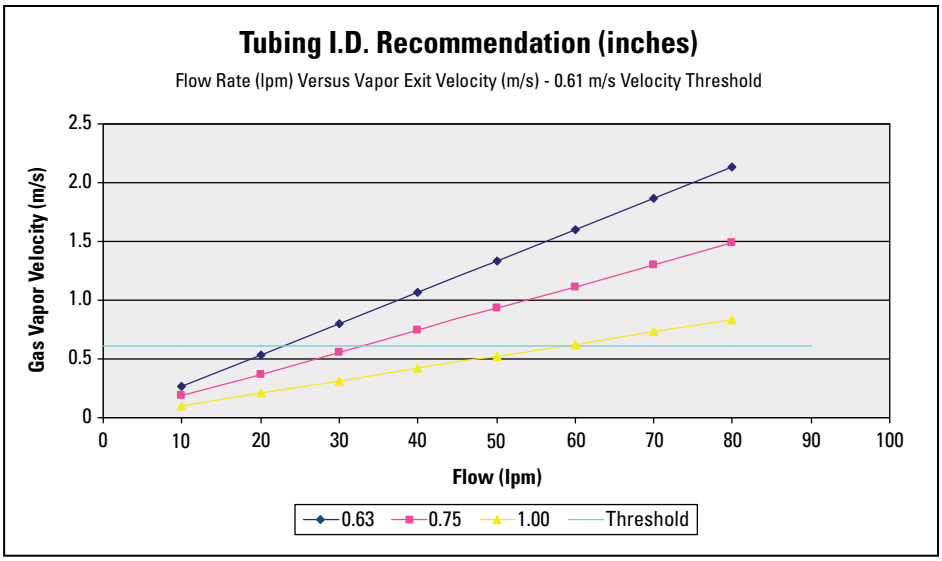


Graph 2.1

NOTE: These results do not take into consideration a "fouling" safety factor. ▲

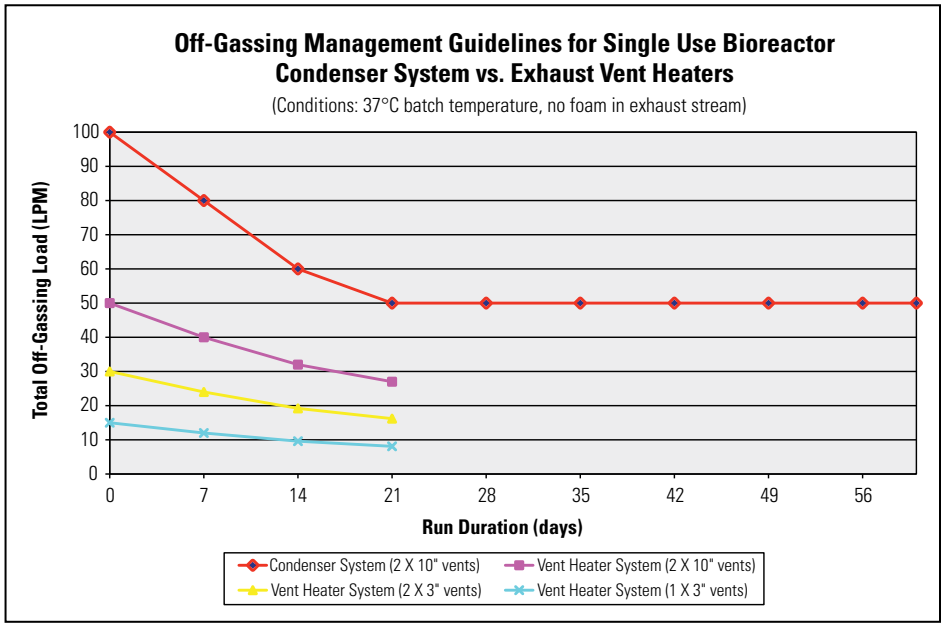
Also consider the size and type of tubing used to connect the exhaust vents to the S.U.B. BPC (when not using an exhaust condenser). Braid reinforced tubing provides the best protection against kinking or accidental pinching of the exhaust line. The 10" vents are supplied with ¾" hose barbs and this tubing diameter will allow condensate to return to the S.U.B. at total off-gas flow rates up to 30 lpm (assuming the tubing is near a vertical orientation). Testing has shown that large diameter tubing will allow for lower exhaust gas velocities and if the vapor velocity is below 0.6 m/s, gravity will allow the condensate formed in the tubing to return to the batch process.

NOTE: Restrictive tubing connectors can create flow bottle necks and ½" ID tubing is typically deemed too small for the 2000 L S.U.B.. ▲



Graph 2.2

Various vent filter configurations are available on the S.U.B. depending upon the process scale and intended application. Graph 2.2 provides a reference for determining the relative capacity of different filters depending upon the amount of gas flow anticipated and the length of the run. In all cases, using a vent filter heater will reduce the chance of condensate blocking the filter but over time suspended solids carried in the exhaust stream will impede the flow of exhaust gas (resulting in increased back pressure). In addition, it is good practice to monitor the amount of foam present in the head space. In all cases, a vent filter heater have very little tolerance for handling the presence of foam in the exhaust stream. A small feed of antifoam (e.g., 10% simethicone, SH30897.02) added directly to the liquid surface of the culture head space typically provides excellent foam control. Large systems (especially the 1000 and 2000 L S.U.B.) can benefit from the use of a disposable condenser system. It has been shown to increase system reliability at high flow rates (beyond 50 lpm) and should warrant strong consideration when performing batch runs beyond 10 days. Results will vary; however, it is strongly recommended that end users select a vent filter configuration providing reserve capacity where possible. For example, dual vent configurations can be used independently with the second filter serving as a redundant backup (providing a quick reserve in case issues arise in process).



Graph 2.2

Condenser System Functional Overview (cont.)

Two operators are required to safely setup the disposable exhaust system. Setup time is typically 2-3 min.

1. The first operator, located at the elevated position, should remove the condenser BPC carefully from the poly-bag packaging and then lower the assembly (directed in a vents first orientation) to the second operator located at ground level, standing to the rear but between the condenser cart and the S.U.B. (Figure 2.108).

2. The first operator at the upper position moves to ground level, opens both doors on the chiller plate, and loads the condenser BPC from the front, keeping the BPC in a saddle bag shape. The vents can hang freely (Figure 2.109).

3. The second operator routes the gas inlet lines around and behind the vent holders and inspects both lines to ensure they are connected to the S.U.B. and are not twisted or kinked, adjusting them as needed (Figure 2.110).

Figure 2.108

Figure 2.109

Figure 2.110

4. The second operator then holds the vent filters, places them into the vent filter holders above the chill plate (Figure 2.111).

5. The first operator then uses the Velcro staps to secure the filters in position (Figure 2.112).

6. The first operator then uses the grasping tabs to position the bag using the two lower button pins on each side of the chiller plate (Figure 2.113).

Figure 2.111

Figure 2.112

Figure 2.113

7. The clear side doors are then closed as the operator carefully manipulates first the gas inlet line and then the gas outlet line (Figure 2.114) to clear the doors as each is closed and latched (Figure 2.115).

8. The second operator then locates the gas inlet lines into the clips behind the vents (Figure 2.116).

Figure 2.114

Figure 2.115

Figure 2.116

9. The first operator loads the peristaltic tubing into the pump, verifying there is sufficient slack at each end of the pump tubing, aligns tubing in the pump channel closes the pump ramp (Figure 2.117).

10. The pump is then started (pushing the red button, Figure 2.118). Operators verify that both the pump and chiller are enabled and running at the proper settings (we recommend that the pump setting be 12-30 RPM and the chiller 5°C). Specified pumping system is qualified to run continuously (wet or dry) beyond 21 days.

Figure 2.117

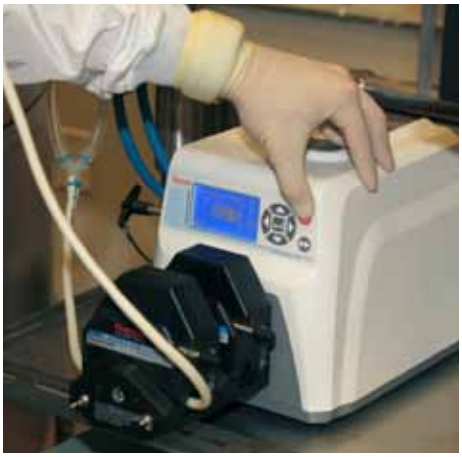


Figure 2.118

11. After setup the operators should verify the following:
    - The elbow fittings on the inlet and outlet of the condenser saddle bag are straight and level
    - The gas inlet line and the condensate line are not twisted, pinched, or obstructed.
    - Low spots in the gas inlet line should be avoided. Adjust the lines to avoid condensation pooling
    - The pump union is loose on both ends of the pump and running smoothly in the peristaltic rollers.

Specific performance questions can be answered by reviewing the Disposable Condenser portion of the S.U.B. Validation Guide or contacting technical support.

Exhaust Vent Heater (optional)

1. A single operator can safely set up the exhaust vents and heaters in this configuration.

2. Clip each filter one at a time into the elevated vent filter holder system; carefully center the filter housing allowing the clip to secure it near the hose barb connections (Figure 2.119).

3. Verify the routing of the exhaust tubing, ensuring that it is not likely to cause kinks in the tubing.

4. Place the vent heaters around each filter ensuring the snap retainers are secured. Position the power leads to avoid interfering with the vent holder brackets (Figure 2.120).

5. Raise and rotate the vent holder bracket as needed. Make final inspection to ensure no kinks or low spots will occur in the tubing between the BPC and the filter (even if the BPC becomes pressurized) (Figure 2.121).

6. Connect the power to the vent heaters and verify operation of controllers.

7. Inspect the controllers' set points (recommended 60˚ C). After 2-5 minutes of operation, verify the vent heaters are warm and near the desired temperature set points and that no alarm indicators are active.

Figure 2.119

Figure 2.120

Figure 2.121

Drive Shaft Insertion

1. The drive shaft is constructed by assembling four pieces; these must be assembled and inserted piecewise in areas having low ceilings.

2. Reminder: The BPC must be filled with enough air to allow for unrestricted loading of the angled drive shaft. Operators should be elevated (i.e. ladder) to effectively assemble and insert the drive shaft.

3. Verify the drive shaft sections and tools are available.

4. Prepare the hollow pass-through by first removing the latch pin on the safety cover (Figure 2.122), opening the safety cover, and removing the threaded cap [turn counterclockwise] (Figure 2.123) of the mixing assembly (Figures 2.124).

Figure 2.122

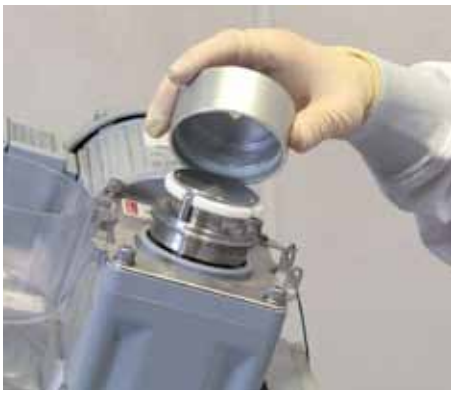


Figure 2.123

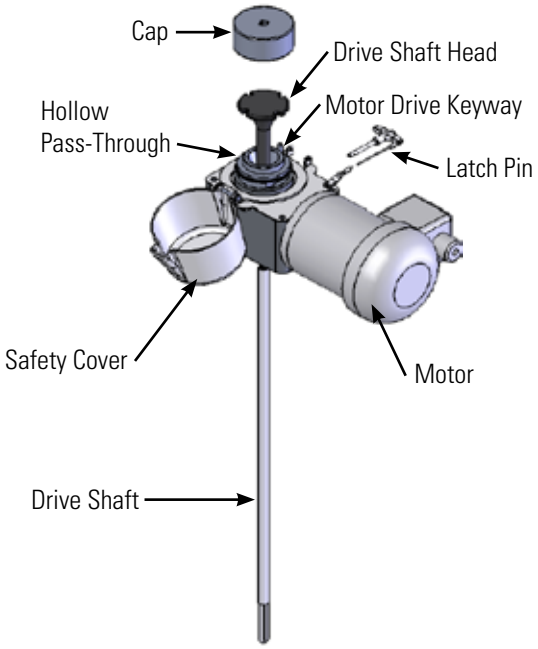


Figure 2.124 Mixing Assembly

Verify the four sections of the drive shaft are located in the drive shaft holders on the side of the outer support container. The sections will be referred to as the upper (section with the drive shaft head), middle – 2 each (section with internal/external quick connect on each end), and lower (section with the square end).

NOTE: No lubrication is required with the quick connect assembly design. ▲

5. First insert the lower section through the hollow pass-through of the mixer drive (Figure 2.125). Once inserted, slide latch pin from mixing assembly into shaft to prevent it from falling into the impeller sleeve (tube), (Figure 2.126).

Figure 2.125

Figure 2.126

6. To connect two shafts together, the button on the female side is depressed (Figure 2.127) and the sleeve is slid back, this will expose a red ring underneath the sleeve (Figure 2.128). This is a visual indicator that the sleeve is not in a locked position.

Figure 2.127

Figure 2.128

7. Place the female side of the quick connect over the male end (Figure 2.129). The connection is fully seated when the red of the male end is no longer exposed (Figure 2.130).

8. Slide the sleeve towards the connection, allowing the push button to lock into position, this will engage the locking mechanism and also cover the red indicator ring (Figure 2.131)

   NOTE: Once fully connected, no red coloring should be visible. This state of no visible red indicates a proper connection. ▲

Figure 2.129

Figure 2.130

Figure 2.131

9. Remove the latch pin, load the partially assembled drive shaft through the hollow pass-through and hold it in position sufficient to allow the latch pin to be inserted in to the next set of holes.

10. Assemble the two middle sections of the drive shaft by joining the segment using the quick connects as performed in the previous steps.

11. Obtain the upper section of the drive shaft and assemble it to the other segment in the manner described previously. Once the sections are secure, remove the latch pin and return the wrenches to the tool holder.

12. Using two hands, carefully guide the completed drive shaft into the BPC using a slight back and forth twisting motion or a counter-clockwise rotation (Figure 2.132).
    - When 2-3" (5.08 cm) of shaft remains, twist slightly to engage the impeller.
    - When 1-2" (2.54 cm) of shaft remains, twist slightly to engage bearing assembly (Figure 2.133).
    - When ~0.25" (0.64 cm) of shaft remains, twist to align motor drive keyway with one of the four outer slots on the drive shaft head (Figure 2.134).

13. Ensure the head is fully seated before directly coupling the drive shaft to the motor by placing the threaded cap back on the hollow pass-through and tightening it.

    NOTE: The cap should be easy to install when the drive shaft head is fully engaged in the hollow pass-through. Otherwise repeat all steps of # 13 before installing cap. ▲

Figure 2.132

Figure 2.133

Figure 2.13

Figure 2.135

14. Secure cap by placing spanner wrench on hollow pass-through and tightening using the supplied torque wrench (Figure 2.135).

    NOTE: The torque wrench is a standard 3/8" square drive and it is calibrated at the factory at 150 in-lbs. ▲

15. Verify wrenches have been removed from the system and returned to the storage holders.

16. Close safety access cover and insert latch pin.

Securing Access Doors

1. The access doors should be secured first with the latches. Proper tension is obtained by adjusting the threaded latch pin. Tension of the latch is adjusted by varying the position of the pin on the threaded shank.

2. The proper latch tension can be obtained by a combination of feel and visual inspection. When closing the latch the handle should begin to provide resistance to closing when the leading edge of the safety pin pass through of the latch handle aligns with the outside edge of the latch base. (Figure 2.136)

   NOTE: When the latch is under-tensioned the safety pin pass through of the latch handle will be covered within the latch base and the handle will close very easily. If the latch is over-tensioned the handle will be excessively difficult to close. ▲

3. For maximum security insert pins (not included) into the respective latches.

4. Turn off the air supply to the overlay line. Insert drive shaft and close side access doors.

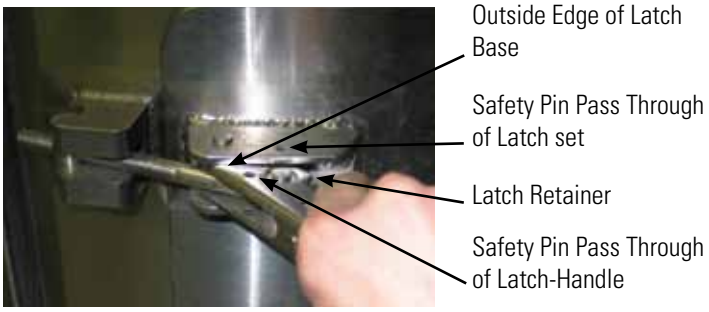


Figure 2.136

Final BPC Installation Steps

1. Verify the proper position of the exhaust filters and that the exhaust flow path is unobstructed. Connect the gas supply lines - verify the intended flow paths for overlay, frit sparges, and open pipe sparge.

2. Verify the overlay and direct sparge lines are well positioned and free of kinks or unintended clamps. Verify the rear access door is closed with proper latch tension.

3. Remove the poly bag from the drain line set and verify redundant line clamps are in position. Use a cable tie around the clamp to ensure the clamp cannot be accidentally opened.

4. Ensure the front access door is latched and align the five Kleenpak ports through the front access window (Figure 2.137). This will be the lower cutout if hardware is supplied with two horizontal slots. Position clamps as close as possible to the bag and close them on all tube ports (Figure 2.138).

5. Place clamps on subsurface lines as close to the port as possible, this will eliminate media from filling these lines prior to use (Figure 2.139).

Figure 2.137

Figure 2.138

Figure 2.139

6. Insert RTD or selected temperature sensor into the thermo-well (Figure 2.140).
   - Place a small amount of glycerol (0.5 mL) in well to aid in heat transfer (Glycerol - Sigma G6279).
   - Sensor should be inserted until base of RTD meets the mouth of the thermo-well.
   - Secure by twisting the luer lock collar if provided. The thermo-well will stretch slightly when RTD is seated (Figure 2.140).

Connect batch-to-tank grounding cable to the stainless steel connector of the sample line (Figure 2.141)

NOTE: Verify all port clamps are closed and located as close as possible to the body of the S.U.B. BPC. ▲

7. **Important: During media fill verify the position of all critical ports (drain, spargers, line sets, and probes) before more than 50 L of liquid is filled into the BPC. This will still allow time for adjustments if it is required after the fill is initiated.**

8. Typically two each fill lines (½" x ¾") and peristaltic pumps are recommended to fill the 2000 L S.U.B. in a timely manner.

Figure 2.140

Figure 2.141

Probe Insertion (2000 L)

1. Probe clips for the 2000 L S.U.B. do not require a probe tray. They clip onto the outer support container and hang from above the probe assembly (Figure 2.142).

2. The probe clip attaches to the tank and is retained using an adjustable ball detent (Figure 2.142).

3. Install presterilized sensor and probe kit using aseptic connection methods as described in Section 2.7.

4. The aseptic connection is completed prior to the bellows being collapsed (Figure 2.143).

Figure 2.142

Figure 2.143

Insert the probe by collapsing the bellows (Figure 2.144).

NOTE: If the BPC is already filled with liquid the best practice is to squeeze the bellows to expel air prior to collapsing it. Now insert the probe fully as described previously. ▲

5. Position the probe clip in the desired horizontal location (Figure 2.145). The clip's adjustable ball detent (spring loaded screw) should be adjusted so the probe clip can be easily moved to the desired position while still securing the clip to the steel support piece.

Figure 2.144

Figure 2.145

6. Swing the probe upward into the flexible spring clip (Figure 2.146). Release the probe assembly and verify the probe remains at the proper insertion depth and angle as the bellows expands to rest freely in the probe clip (Figure 2.147).

Figure 2.146

Figure 2.147

NOTE: The fixed position of the probe clip and the flexible nature of the spring retainer allow for both proper angle (>10 degrees) and compression of the probe bellows. ▲

2.5 Probe Assembly

Preparation and Sterilization

1. Select the appropriate probe (see Section 1). Verify the presence of a Teflon support ring and O-ring on the probe and visually inspect them for damage.
2. Perform any required probe maintenance and calibrate the pH probe (see Probe Calibration within this section).
3. Insert the probe into the probe assembly through the threaded adaptor.
4. Verify the probe tip is not touching (>1/4" [6.35 mm] gap) the membrane of the Kleenpak Connector before threading into probe adaptor.
5. Hand tighten the adaptor and verify the probe tip is not touching the membrane.
6. Place the probe assembly with probe into the autoclave tray for probe kits (Figure 2.148).
7. Autoclave the probe assembly using a validated sterilization cycle (approximately 30 minutes at 122°C). Thirty minute sterilization cycles are generally sufficient. Options of wet or dry cycle parameters can be used. Slow exhaust cycles are preferred as this minimizes stress on the probes during the temperature and pressure changes of autoclaving.
8. Allow sufficient time for probe assemblies to cool completely before seeking to connect to the S.U.B. bag for probe insertion.
9. When stored properly, the autoclaved probe assemblies can be stored dry for short periods of time (< 24 hr) without loss of sensor longevity, performance or sterility.

NOTE: Before beginning probe insertion, please become familiar with the Kleenpak Connector procedure outlined in Section 2.7. ▲

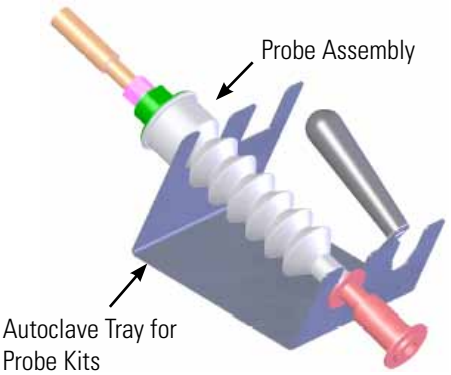


Figure 2.148

Probe Insertion (50 - 1000 L)

1. Insert probes into S.U.B. BPC using autoclaved probe assemblies.
   a. Place tubing clamps on all probe ports prior to attempting to connect probe assemblies (this will prevent sterility loss in case errors are made during connection of Kleenpak Connectors) (Figure 2.149).

Figure 2.149

   b. Position probe support plate onto outer support container. This holds the probes at a 15 degree incline for best performance (Figure 2.150).

Figure 2.150

   c. Connect Kleenpak Connector using protocol outlined by the manufacturer (Section 2.7).
   d. Ensure all four snaps click on each connector and the base and barrel of Kleenpak is fully seated.
   e. Remove tubing clamp on the individual probe port.
   f. Insert probe by collapsing bellows toward S.U.B. (Figure 2.151).

Figure 2.151

   g. Probe is seated when bellow is fully collapsed. A small amount of fluid may enter the bellow if the probe is loaded after media fill.

2. Secure probe by placing connected probe assembly first into probe holder (Figure 2.152) and then locking the holder into probe support shelf.
    a. Begin by placing the entire collapsed probe assembly in the probe holder starting with the Kleenpak Connector side being placed in the holder side with the short fingers.
    b. If necessary, compress the probe bellows further to allow the probe assembly to be positioned and locked into the other end of the probe holder (Figure 2.153).
    c. Allow probe bellows to relax. This secures the probe between the probe holder fingers.
    d. Align probe holder with alignment holes of the probe support shelf.
    e. Press downward and into the slots closest to the S.U.B. BPC, then slide the holder backward slightly to lock the probe holder into the probe support shelf.

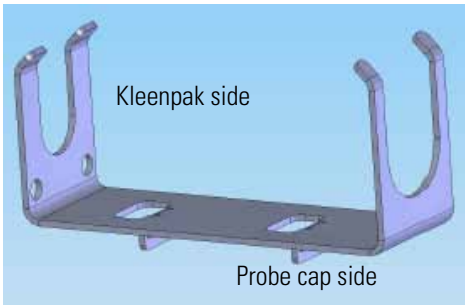


Figure 2.152

Figure 2.153

NOTE: Probe ports that are not used prior to media fill must remain clamped. Probe ports not used at the initiation of the run can be accessed later for probe replacement or redundancy purposes if required. ▲

Probe Calibration

Probe calibration is controller specific; however, the following general rules apply:

a. pH probes must be calibrated prior to steam sterilization and the calibration of the probe can be standardized by comparison of an off-line sample once the pH probe has been connected to the S.U.B.
b. Dissolved oxygen probes are generally calibrated post steam sterilization. Once the probe is connected to the S.U.B. and is allowed sufficient time to polarize (6-8 hours of continuous connection to the power supply provided by a controller or polarization module), it can be calibrated.

2.6 Single-Use Bioreactor BPC Sampling

Sampling

During operation of the S.U.B., samples may need to be taken for monitoring of various parameters established by the user. The following describes two techniques for sampling: aseptic sampling via sterile syringe and sampling utilizing a sterile manifold.

Aseptic Sampling

Using standard luer lock on 60 mL syringe or sterile manifold:

1. Remove dust cover from SmartSite (Figure 2.154)
2. Clean SmartSite with sanitary wipe
3. Connect sanitary luer lock type syringe (Figure 2.155)
4. Apply small amount of vacuum pressure by pulling out syringe plunger slightly
5. Open pinch clamp and pull sample (approximately 30-60 mL) using care not to allow any back flow
6. Close pinch clamp and remove syringe (this will be a purge sample)
7. Clean SmartSite with sanitary wipe
8. Connect sanitary luer lock type syringe
9. Apply small amount of vacuum pressure by use of syringe
10. Open pinch clamp and pull desired sample volume (approximately 10-20 mL) using care not to allow any back flow
11. Close pinch clamp and remove syringe (this will be a representative sample)
12. Clean SmartSite with sanitary wipe and replace dust cap

Figure 2.154

Figure 2.155

Sampling with Sterile Manifold

Figures 2.156 and 2.157:

1. Remove manifold from protective poly-bag package
2. Close all clamps on manifold lines
3. Use sterile tubing welder to connect manifold to sample line
4. Inspect welds and open flow path by pinching the welds
5. Open two clamps at inlet and the clamp at purge bag (100 mL pillow bag)
6. Purge sample line by filling this bag (recommended 30-60 mL)
7. Close clamp nearest purge bag
8. Open clamp to sample bag (50 mL pillow bag)
9. Allow bag to fill with liquid by gravity (recommended 10-20 mL)
10. Close clamps at sample manifold inlet
11. Close clamp nearest the sample bag
12. Remove the filled manifold from S.U.B. by welding new manifold onto sample line (this will be used for taking the next sample)

Figure 2.156

Figure 2.157

2.7 Pall Kleenpak Connector Instructions

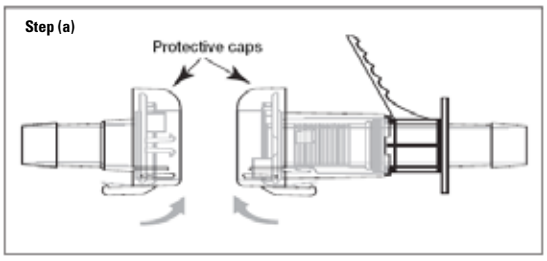
These instructions and the information contained within must be read thoroughly as they contain valuable information gained by extensive experience. It is very important that all instructions are carefully followed and where appropriate they should be incorporated into the end user's standard operating procedures. If some of the procedures do not suit your needs, please consult Pall or your local distributor before using Kleenpak connectors. Use of this product in a manner other than in accordance with Pall's current recommendations may lead to injury or loss. Pall cannot accept liability for such injury or loss.

Installation and Operation
Training on the proper assembly and recommended uses of the Kleenpak connector is necessary.

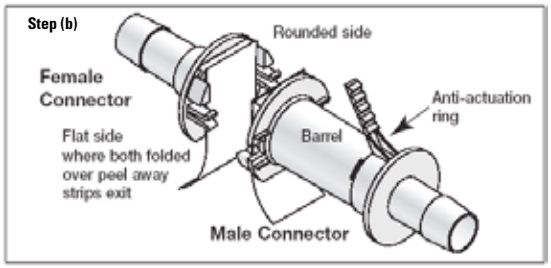
- Before installation, it is essential to verify that the Kleenpak connector selected is suitable for the fluid to be processed and has been sterilized appropriately.
- Complete assembly procedures and technical specifications for Kleenpak connectors are contained in Pall publication USD 2233d.
- Please follow carefully the instruction below.

Pall Kleenpak Connector (Standard Instructions)

a. Lift and pull tab of protective caps to remove caps from connectors.

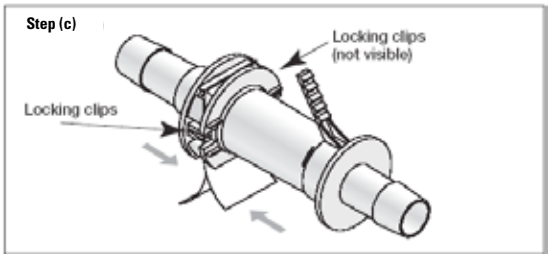


b. Hold the barrel of the larger (male) connector above the base. Align the smaller (female) connector with the larger (male) connector so that both folded white peel away strips are facing the same direction as they exit out the flat sides of the connectors.

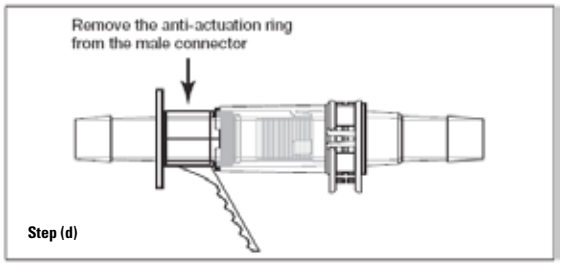


NOTE: Rounded sides must be in alignment and the white peel away strip must remain folded. If the connectors are not aligned properly, the connection cannot be made. The peel away strips must remain folded. ▲

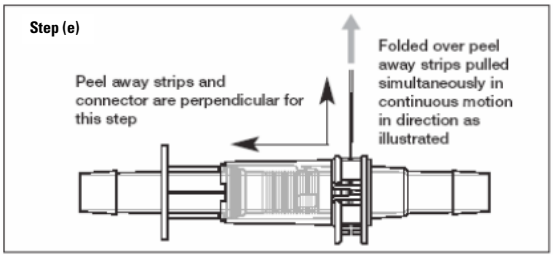
c. Once aligned correctly, press the two connectors together firmly until both sets of locking clips snap together tightly.



d. While holding the Kleenpak Connector securely in hand, pull the anti-actuation ring outward.

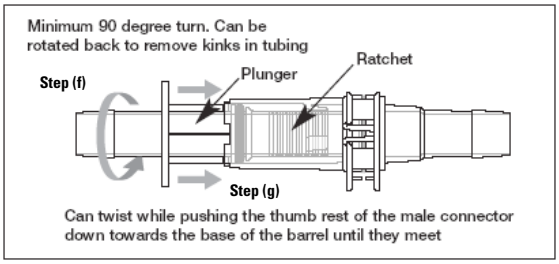


e. With one hand, hold the barrel of the male connector. Using the other hand, grasp both white peel away strips as close as possible to the flat side of connector to ensure a good grip and pull them out simultaneously in a smooth continuous motion. Ensure that the connector is perpendicular to the peel away strips shown in illustration for Step (e). The perpendicular orientation must be maintained while the two strips are pulled simultaneously. Do not use if only one white peel away strip is removed accidentally instead of two; this will affect the sterility of the pathway.



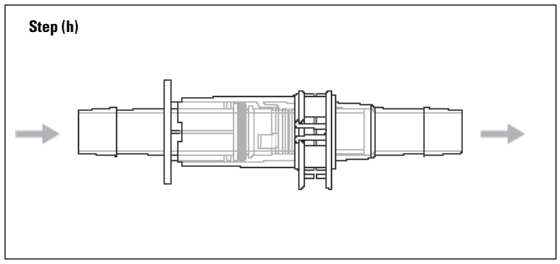
NOTE: Do not impart radial force on the connector. A radial force can cause the connector to break. If a radial force is present due to items attached to the connector, then the connector must be properly supported. ▲

f. Rotate the thumb rest on the male connector one full turn at least 90 degrees in the clockwise direction. The rotation serves to bend the anti-actuation tabs, which prevents inadvertent engagement. If required, the thumb rest can be turned counterclockwise to remove kinks in the tubing.



g. Push the thumb rest of the male connector down towards the base of the barrel until they meet. If the thumb rest has not already been turned counterclockwise to remove tubing kinks, the thumb rest can be turned counterclockwise while it is being pushed towards the base of the barrel.

NOTE: In order to establish a proper connection the plunger inside the male connector must be fully inserted into the female connector. As a verification, this normally occurs when the last or second to last rings on the plunger locks into the ratchet. Minimally, the second to last ring must be locked into the ratchet to ensure a proper connection. The thumb rest can be turned one full turn back to re-align tubing, as required, if the second to last ring is locked into ratchet. If the plunger has been pushed further than the second to last ring, then it may not be possible to turn the thumb rest. ▲



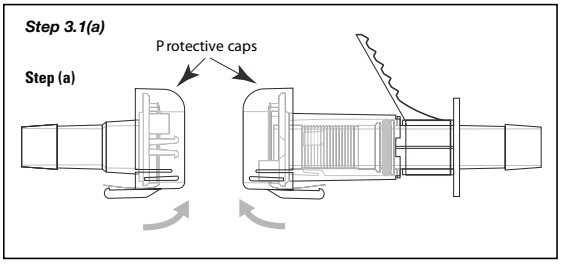
h. Start the fluid transfer.

Pall Kleenpak Connector (Instructions for use with assembly aid)

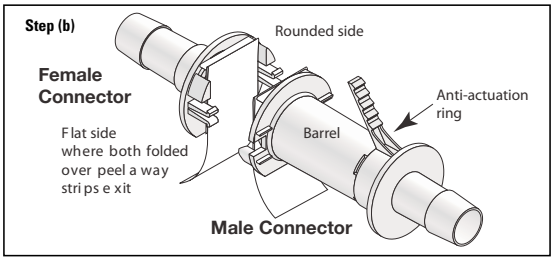
Receipt of the Equipment
The connector assembly aid is provided non sterile and can be reused multiple times. It needs to be stored in clean and dry conditions between each use.

Connect both halves of Kleenpak connector together

a. Lift and pull tab of protective caps to remove caps from connectors.

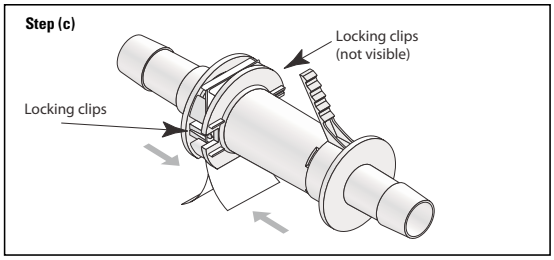


b. Hold the barrel of the larger (male) connector above base.
   - Align the smaller (female) connector with the larger (male) connector.
   - Flat sides should be aligned.
   - Both peel away strips must remain folded and oriented in the same direction.



NOTE: If the connectors are not aligned properly, the connection cannot be made. ▲

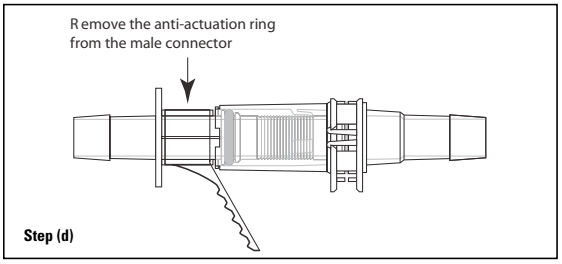
c. Once aligned correctly, press the two connectors together firmly until both sets of locking clips snap together tightly.



WARNING: A KLEENPAK CONNECTOR WILL NOT FIT INTO THE ASSEMBLY AID IF THIS CONNECTION IS NOT PROPERLY SECURED. ▲

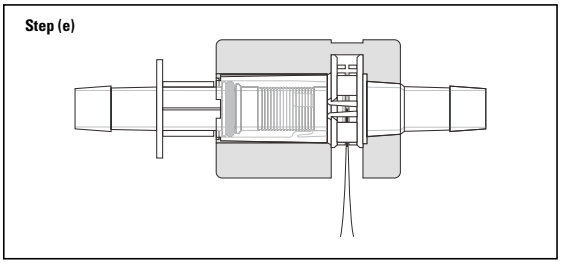
Remove Anti-Actuation Device

d. While holding the Kleenpak Connector securely in hand, pull the anti-actuation ring outward.



Install into Assembly Aid

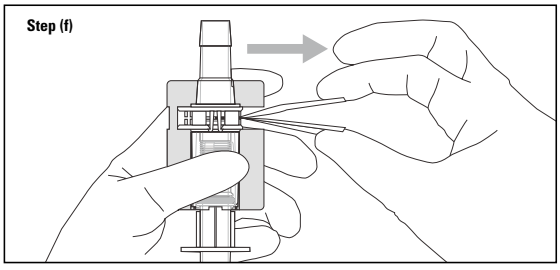
e. Place connected Kleenpak Connector unit firmly into assembly aid so that both membrane strips protrude through the opening and are easily accessible for removal.

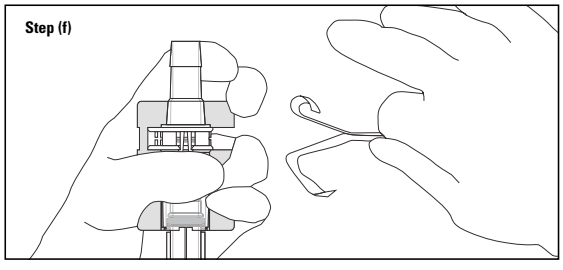


WARNING: KLEENPAK CONNECTOR SHOULD STAY SECURELY IN THE ASSEMBLY AID WHEN PROPERLY INSTALLED. ▲

Remove Membrane Strips

f. Hold assembly aid in the palm of hand with Kleenpak Connector exposed outward, and thumb is supporting the Kleenpak Connector in the unit. Using the other hand, firmly grasp both white peel away strips as close as possible to the body of the assembly aid to ensure a secure grip and pull them out simultaneously in a smooth continuous motion. Ensure that the connector is perpendicular to the peel away strips.



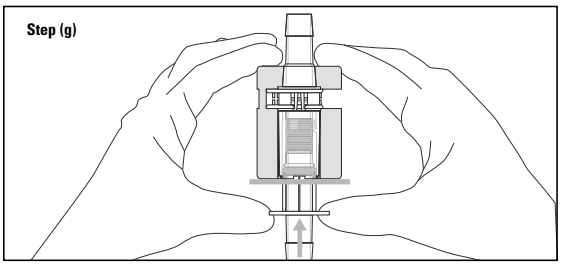


WARNING: DO NOT USE IF ONLY ONE WHITE PEEL AWAY STRIP IS REMOVED ACCIDENTALLY INSTEAD OF TWO; THIS WILL AFFECT THE STERILITY OF THE PATHWAY. ▲

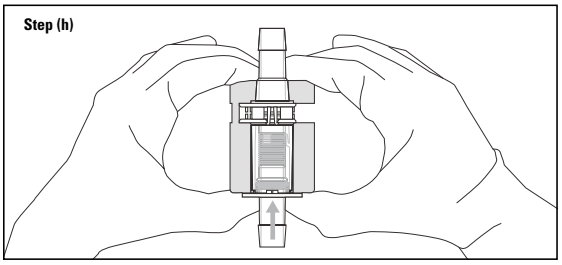
Complete Flow Path Actuation

g. With Kleenpak Connector still secured in the assembly aid, rotate and push the thumb rest of the male connector down towards the base of the barrel until they meet.

NOTE: In order to establish a proper connection, the plunger inside the male connector must be fully inserted into the female connector. ▲



h. The thumb rest can be turned one full turn back to re-align tubing, as required.



WARNING: VERIFY THAT THE PLUNGER HAS BEEN FULLY INSERTED INTO OPPOSING CONNECTION BY USING THE ASSEMBLY AID EDGE AS A GAUGE UPON COMPLETE ACTUATION. ▲

Process

l. The Kleenpak Connector assembly is now complete and assembly aid may be removed.

Section 3 Specifications

This section covers the following information:

3.1 50 L Single-Use Bioreactor

Data Sheet 026 Rev 10

Thermo Scientific HyClone Single-Use Bioreactor (S.U.B.) 50 L

The Thermo Scientific HyClone Single-Use Bioreactor (S.U.B.) is the leading single-use alternative to conventional stirred tank bioreactors for animal and insect cell culture. The current range includes units with maximum working volumes of 50, 100, 250, 500, 1000 and 2000 L. The S.U.B. is now available with new optimized standard BioProcess Containers with improved dual sparge capability. Open pipe and frit sparging systems are now included to provide a wider range of operating conditions.

Overview:

The HyClone® S.U.B. provides all the advantages of single-use bioprocessing without having to buy a complete new bioreactor system. The critical design parameters of the S.U.B., such as height to diameter ratios, mixer design and location and typical control system interfaces, have been maintained.

The S.U.B. BioProcess Container™ (BPC®) is supplied sterilized by irradiation and therefore does not require any facility hook-ups for sterilization or cleaning. A key element to the single-use design is the plastic (polyethylene) impeller with a bearing/seal assembly linked to an external mixer drive.

50 L Water Jacket S.U.B.

This document covers S.U.B. systems with a maximum working volume of 50 L and the new optimized standard S.U.B.s with dual sparge capability which provide a wider range of k_La values, better pH control and lower foaming than the original disk sparger.

The S.U.B. system consists of the following components:

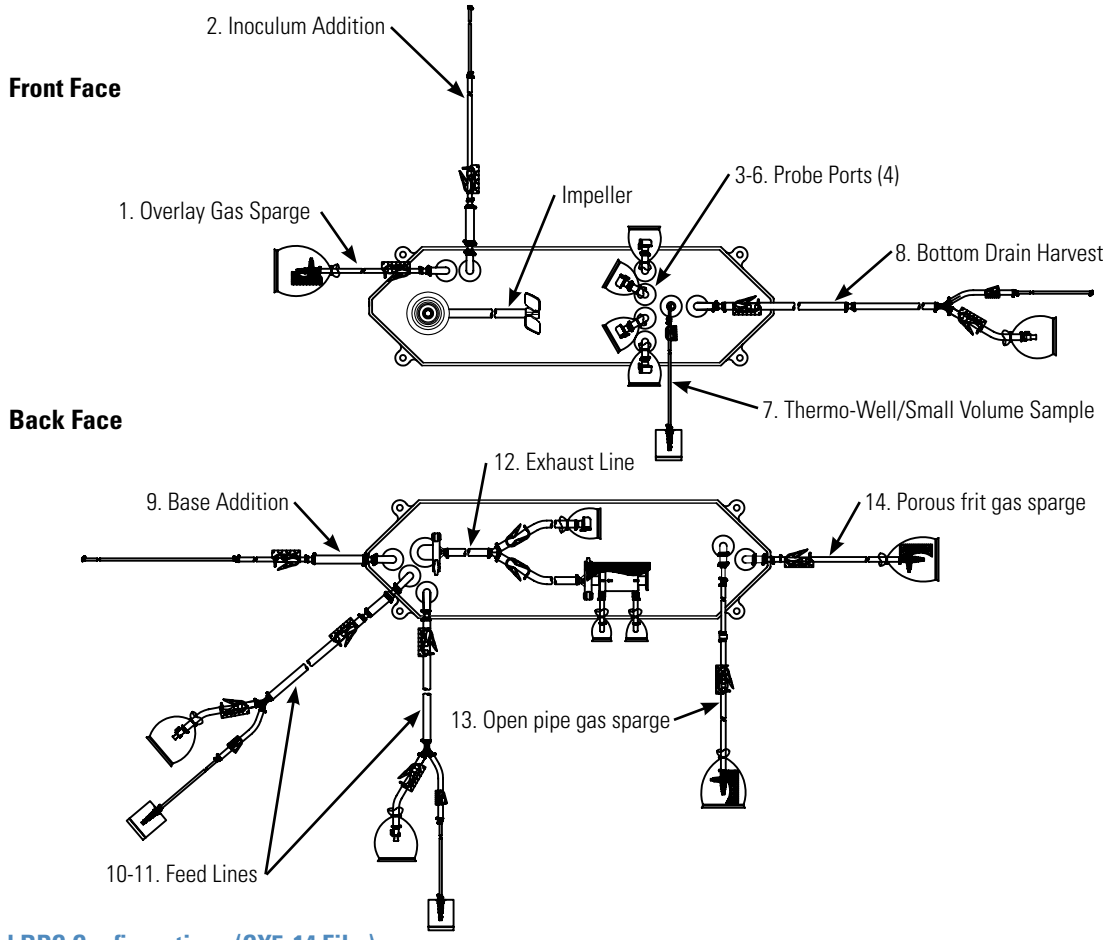
1. Outer Support Container—with a mixer drive complete with control unit and an electrical heater or water jacket.
2. Single-Use Bioreactor BPC—complete with agitator assembly, sparger, vent filter inlet and outlet ports, plus ports for integration of sensor probes and line sets. The S.U.B. BPC is supplied sterile and ready-to-use.
3. Drive Shaft—inserted into the S.U.B. BPC through the mixing drive motor and locked into the disposable agitator assembly.
4. Process Controls—temperature (not on water jacket) and agitation control are integrated into the S.U.B., but additional pH or dissolved oxygen (DO) controls must be supplied by the user.

Item	50 L Electric Resistive Heater	50 L Water Jacket
Rated Liquid Working Volume	50 L	
Minimum Liquid Working Volume	25 L	
Total Reactor Volume (Liquid & Gas)	65.5 L	
BPC Chamber Diameter	13.75" (34.9 cm)	
BPC Chamber Shoulder Height	31.5" (80 cm)	
Liquid Height @ Rated Working Volume	20.5" (52.1 cm)	
Overall Reactor Geometry (height/diameter ratio)	1.9:1	
Fluid Geometry @ Working Volume (height/diameter ratio)	1.5:1	
Impeller (quantity x blade count)	1 x 3	
Impeller Diameter	4.63" (11.75 cm)	
pH & DO Probe— Autoclavable Type (Applisens, Broadley James, Metler Toledo)	12 mm diameter x 215-235 mm insertion length x 13.5 PG thread	
Hold-Up Volume	< 0.5 L	
Electrical Power Supply Requirement (voltage, phase, amp)	120/240 VAC, single, 20/10 A	
Overall Width	25.9" (65.7 cm)	23" (58.4 cm)
Overall Length	36.1" (91.7 cm)	36" (91.4 cm)
Overall Height	52.8" (134 cm)	52.5" (133.4 cm)
S.U.B. Recommended Operating Parameters		
Operating Temperature Range	Ambient to 40 +/- 0.1°C (104 +/- 0.2°F)	
Motor Speed	30-200 rpm	
Volume Range	25-50 L	
Maximum Bag Pressure	0.5 psi (0.03 bar)	
Continuous Operating Time	21 days*	

*Mixing time at nominal volume only.

Standard BPC Configurations (SH30774.01)

For use with tubing welder and CPC Quick Connect



Standard BPC Configurations (CX5-14 Film)

For use with tubing welder and CPC Quick Connect

Line	Description	Tubing Set (ID X OD X Length)	End Treatment
1	Overlay Gas Sparge	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex® X 6" (15 cm)	Hydrophobic vent filter with Emflon® II
2	Inoculum Addition	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 60" (152 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm)	Plugged
3-6	Probe Ports (4)	1/2" (12.7 mm) Tube ports	Pall® Kleenpak™ aseptic connectors—KPCHT Series (Female)
7	Thermo-Well/ Small Volume Sample	Thermo-Well Adapter for 1/4" (6.4 mm) Diameter. 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 18" (46 cm)	SterilEnz® Pouch with injection site assembly
8	Bottom Drain Harvest	1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 60" (152 cm) reduced to 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 12" (30 cm) splits to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 12" 30 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm) and 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 12" (30 cm)	Plugged 3/8" MPC Insert
9	Base Addition	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 6" (15 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 60" (152 cm)	Plugged
10-11	Feed Lines	3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 60" (152 cm) splits to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 12" (30 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm) and 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 12" (30 cm)	SteriEnz Pouch with injection site assembly 3/8" MPC Body
12	Exhaust Line	1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 6" (15 cm) splits to 1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 6" (15 cm) and 1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 10" (25 cm)	Pall Kleenpak aseptic connector—KPCHT Series (Female) Pall Kleenpak 0.2 Micron Exhaust Vent Filter
13	Open Pipe Gas Sparge	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 3" (8 cm) reduced to Check Valve and 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 48" (122 cm)	Hydrophobic vent filter with Emflon II
14	Porous frit gas sparge 12 mm dia (25 µm pores)	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 6" (15 cm) reduced to Check Valve and 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 48" (122 cm)	Hydrophobic vent filter with Emflon II

Ordering Information for Standard BPC Products

Custom BPC Options:

Category	Options/Capability	Remarks
Tubing Type	C Flex, platinum cured silicone, PVC, Pharmed®, PharmaPure®	More information in selection guide of BPC catalog
Tubing Size	Specific lengths of 1/8" ID to 1" ID	ID limitations due to port size
Connectors	Luers, CPC Quick Connects, SIP connectors, Triclamp, Kleenpak, Lynx®, SmartSite®, Clave®, Lynx steam thru, CPC Steam Thru, Gore steam valve, Gore Mini TC, BioQuate (GE), PAW SterilEnz®, end plug, etc.	Refer to selection guide in BPC catalog for further information by connection type. **Note:** Only option for probe port connections is Kleenpak.
Kleenpak (i.e., probe) ports	Additional ports: second row of 4 for 50 L to 250 L S.U.Bs.; second row of 5 for 500 L and 1000 L S.U.B.s	
Disposable sensors	Pressure sensor: Pendotech for 50 L to 250 L S.U.B. (comes standard on 500 L and 1000 L) DO – Finesse DO and pH – PreSens Availability of various other disposable sensors currently pending.	
Addition of ports/lines (other than 2nd row of probe ports)	Limited engineer-to-order customization possible such as additional media lines and vent filter lines. Requires economic justification.	Dependent on location in bag and compatibility with hardware
Port sizes	Limited customization possible as engineer-to-order with justification.	Dependent on location in bag and fit with hardware (e.g., 1" ID port on harvest line)
Re-arrangement of lines on existing ports	Limited customization possible, e.g., moving sample/tempwell port to a probe tube port, or swapping overlay inlet line with supplement line.	Dependent on location in bag and fit with hardware
Sparger	Dual sparger (open pipe plus porous frit) standard. Can do an engineer-to-order for one or the other alone. Make-to-order bags will be built around standard dual sparger chamber.	
Dip tube lines	Limited customization possible. Suggested use through 1" port, so this is engineer-to-order. Otherwise must use ferrule approach.	Length cannot interfere with impeller and shaft. Typical is 10" or shorter.
Overlay and Sparge Line Filters	Can use disposable (capsule) filter other than standard hydrophobic vent filter with Emflon II.	
Vent Filters	Standard is Pall Kleenpak 0.2 micron exhaust vent filter.	**Note:** Vent filter heater configuration restricts options
Vent Filter Tubing Length	Extended filter height above the S.U.B. bag is make-to-order.	Must be compatible with a vent filter bracket option
Filters on Media and Supplement Inlets	Choice of filters for inlets used to sterile filter incoming media or supplements.	

Please Note: Not all options are available for all ports. No customization of port type and location, chamber dimensions or mixing assembly is possible. For additional information, please see the Selection Guides in the S.U.B. BPC Catalog.

Presentation (as dry BPC systems):

Outer Packaging	Supplied 'flat-packed' Two polyethylene outer layers
Label	Description Product code Lot number Expiry date on outer packaging and shipping container
Sterilization	Irradiation (25 to 38 kGy) inside outer packaging
Shipping Container	Durable cardboard carton
Documentation	Certificate of Analysis provided with each lot for each delivery

Hardware Standard Products

Electric Resistive Heater:

Part Number	Description	
SV50171.01	50 L S.U.B., US version (120 VAC, Single Phase)	Includes: 304 stainless steel outer support container with swivel caster platform, variable speed agitation controller, motor, drive assembly with shaft, PID temperature controller, RTD sensor, integrated resistive heating element, probe shelf and standard tool set
SV50171.02	50 L S.U.B., EU version (240 VAC, Single Phase)	

Water Jacket:

Part Number	Description	
SV50171.03	50 L S.U.B., US version (120 VAC, Single Phase)	Includes: 304 stainless steel outer support container with swivel caster platform, variable speed agitation controller, motor, drive assembly with shaft, RTD sensor, integrated water jacket, probe shelf and standard tool set
SV50171.04	50 L S.U.B., EU version (240 VAC, Single Phase)	

Custom Options

Custom Hardware Options:

For stainless steel capabilities, please contact your sales representative for HyClone products for more information.

Accessories

Part Number	Description	
SH30720.01	Bioreactor Probe Assembly (non-sterile)	Used to package the pH and DO probes (not supplied) for sterilization and to aseptically connect them to the S.U.B. BPC. See Figure 1.
SV20664.01	Heavy Duty Tubing Clamp	Reusable tubing clamp used on probe ports when connecting probe assemblies.
SV20664.02	Heavy Duty Tubing Clamp (4 pack of SV20664.01)	
SV20664.03	Heavy Duty Tubing Clamp (10 pack of SV20664.01)	
SV20750.01	S.U.B. Temperature/Sample Port	Used for RTD calibration/validation.
SV50177.01	Autoclave Tray for Probe Kits (stainless steel)	Support tray which allows the probes to be safely autoclaved. See Figure 2.
SH30845.01	Sterile Sampling Manifold with luer lock (individual)	Available for aseptic luer connection or weld onto the sample line to take sample sets.
SH30845.02	Sterile Sampling Manifold with luer lock (10 pack)	
SV50177.65	Frit Sparge Line Support	Recommended to maintain the frit sparge in a vertical position.
SV50177.16	Elevated Filter Bracket	Needed to support an elevated vent filter.

Figure 1
Bioreactor Probe Assembly

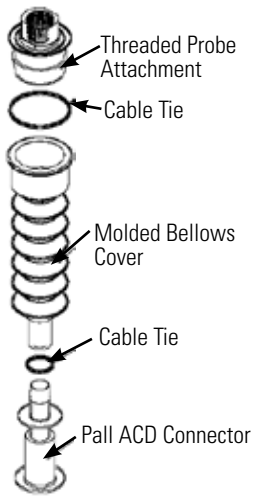
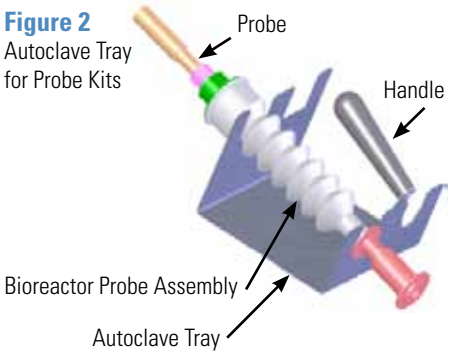


Figure 2
Autoclave Tray for Probe Kits

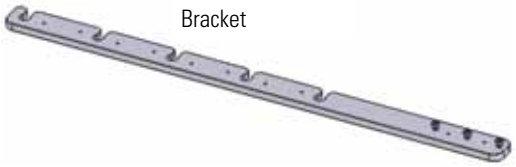


Additional information on autoclave tray:

- Fabricated from stainless steel
- Plastic carry handle for easy transport right out of the autoclave
- Positions probes on 15% incline for greater probe/membrane longevity
- Will restrain probe bellows from collapsing during sterilization
- Probe holder accommodates two probes

Figure 4
Frit Sparge Line Support

Figure 3
Elevated Filter Bracket



Single-Use Bioreactor (S.U.B.) First Time Operator—Recommended Parts List

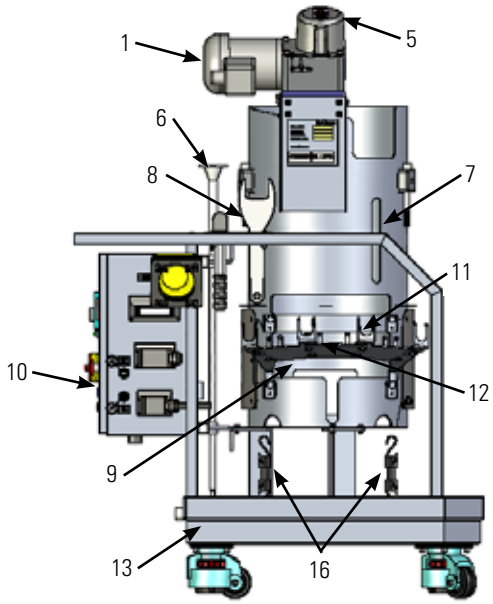
Available Parts (consumables sufficient for three complete cell culture runs)		
Part Number	**Description**	**Quantity**
SV50171 (50 L)	S.U.B. Hardware System (standard)	1
SH30774.01	S.U.B. BPC (standard)	3
SH30720.01	Bioreactor Probe Assembly (non-sterile for use in autoclave)	12
SV20664.03	Heavy Duty Tubing Clamp (10 pack)	1
SV50177.01	Autoclave Tray for Autoclaving Probe Kits	2
SV20750.01	S.U.B. Temperature Port (used to verify RTD calibration)	1
SH30845.02	Sterile Sampling Manifold with Luer Locks (10 pack)	3
Auxiliary Components Supporting The Single-Use Bioreactor		
Description	**Purpose**	**Quantity**
Bioreactor control system	Necessary for regulation of gas pressure and flow rate control for DO and pH set points	1
DO probe	Autoclavable Probe (13 mm X 13.5PG thread w/ 195-235 mm insertion length)	1
pH probe	Autoclavable Probe (13 mm X 13.5PG thread w/ 195-235 mm insertion length)	1
Sterile/Aseptic Connection Method	Tubing Welder (Terumo or Wave), Steam In Place (SIP) Sterilizer, or Laminar Flow Hood	1
Peristaltic Pump	Used for fluid transfer between line sets and containers	1
Temperature Control Unit (TCU)	Necessary for water jacket temperature control (not provided)	1

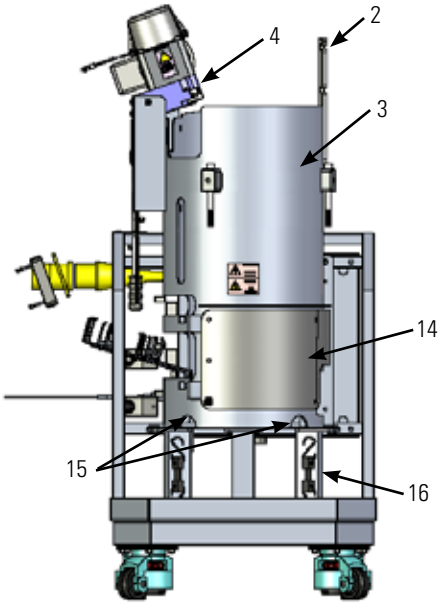
Hardware Features

50 L with Resistive Heater:

The stainless steel outer support container contains the following features:

1. Mixer motor
2. Exhaust vent filter holder
3. Stainless steel (304) outer support container
4. Bearing port receiver with clamp
5. Mixing assembly with shield
6. Drive shaft
7. Liquid sight window
8. Standard tool set
9. Probe access window
10. Control panel
11. Probe holder
12. Probe shelf
13. Platform with swivel casters and leveling pads
14. Resistive heater w/heat shield
15. Bottom cut outs for BPC alignment
16. Stretch hooks



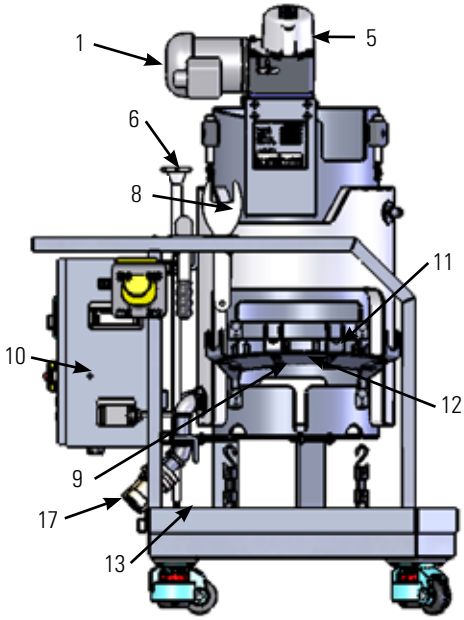


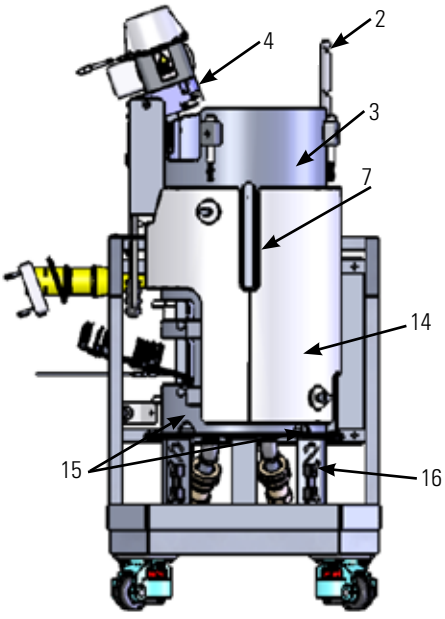
Hardware Features

50 L with Water Jacket:

The stainless steel outer support container contains the following features:

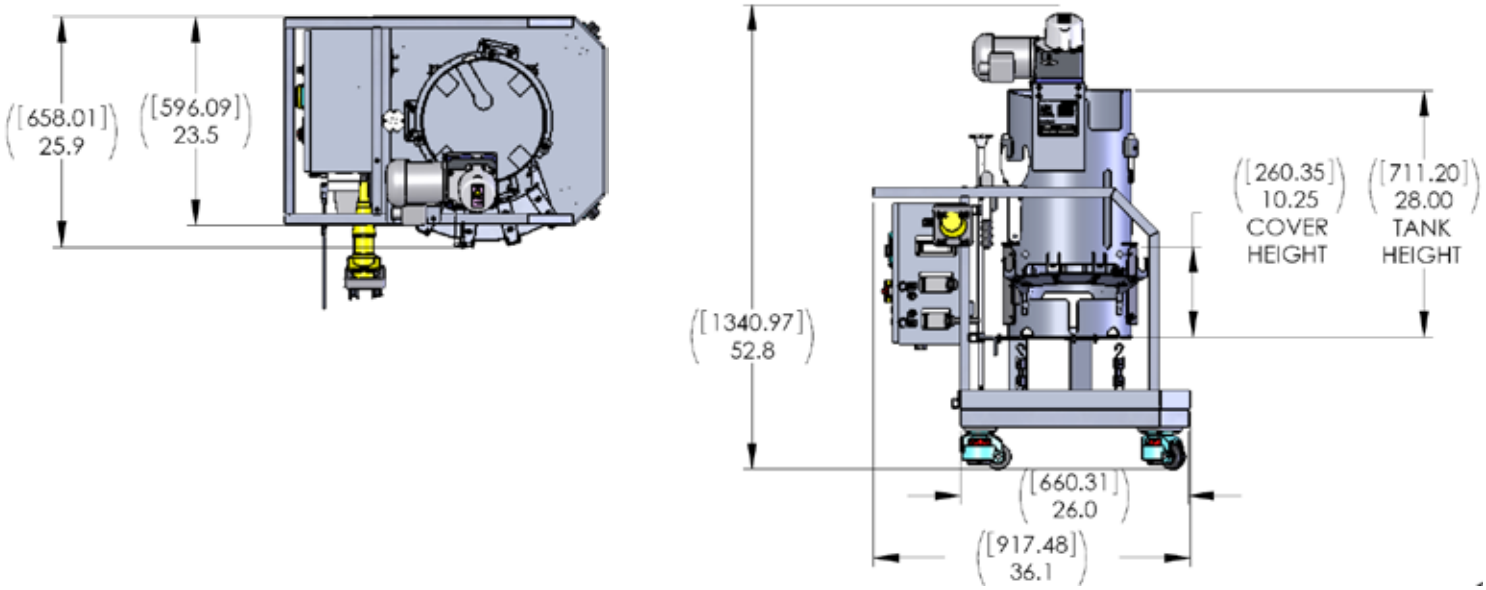
1. Mixer motor
2. Exhaust vent filter holder
3. Stainless steel (304) outer support container
4. Bearing port receiver with clamp
5. Mixing assembly with shield
6. Drive shaft
7. Liquid sight window
8. Standard tool set
9. Probe access window
10. Control panel
11. Probe holder
12. Probe shelf
13. Platform with swivel casters and leveling pads
14. Laser dimple water jacket
15. Bottom cut outs for BPC alignment
16. Stretch hooks
17. Jacket quick connect couplings



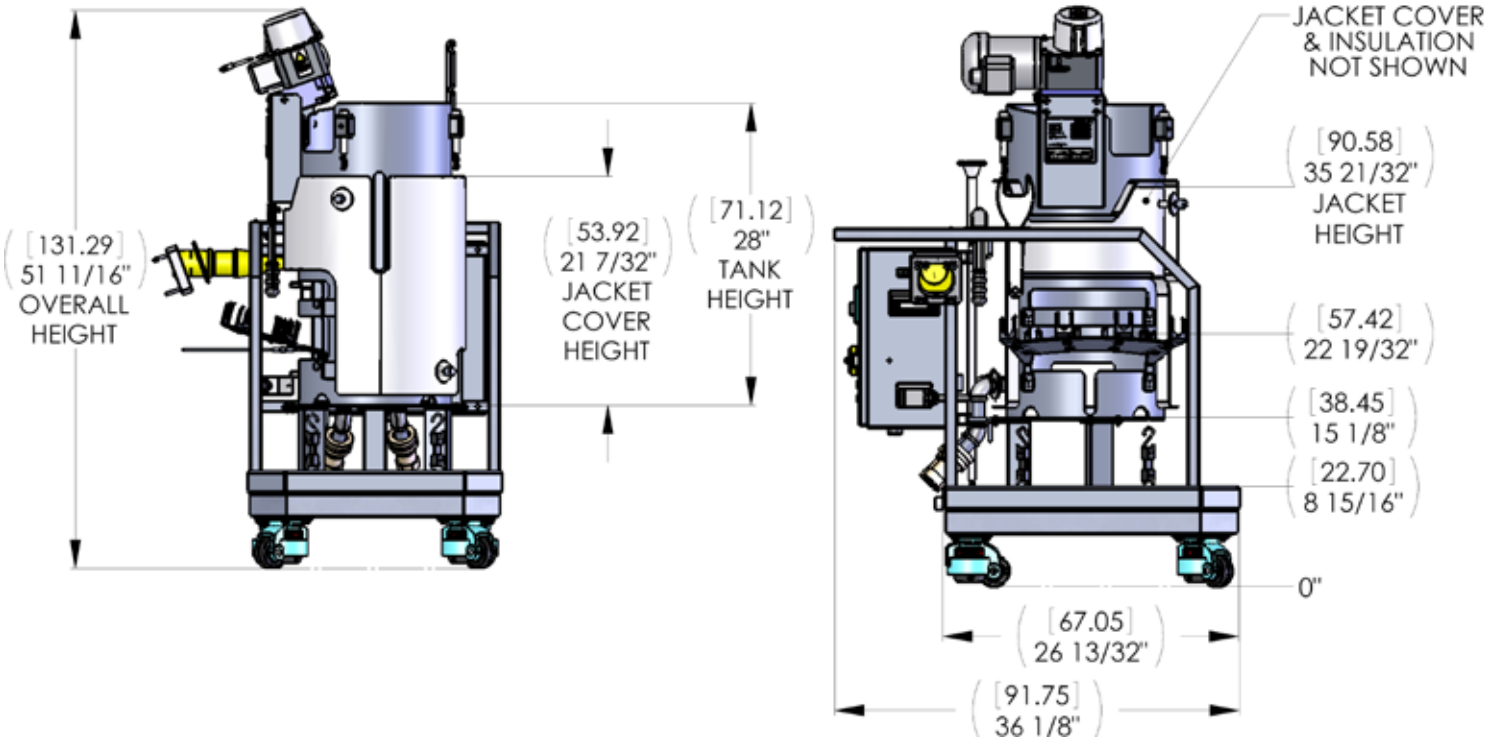


Outer Support Container (units in inches [mm])

50 L S.U.B. Electric Resistive Heater:



50 L S.U.B. Water Jacket:



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Thermo SCIENTIFIC

3.1.2 50 L Hardware Specifications Electric Resistive Heater

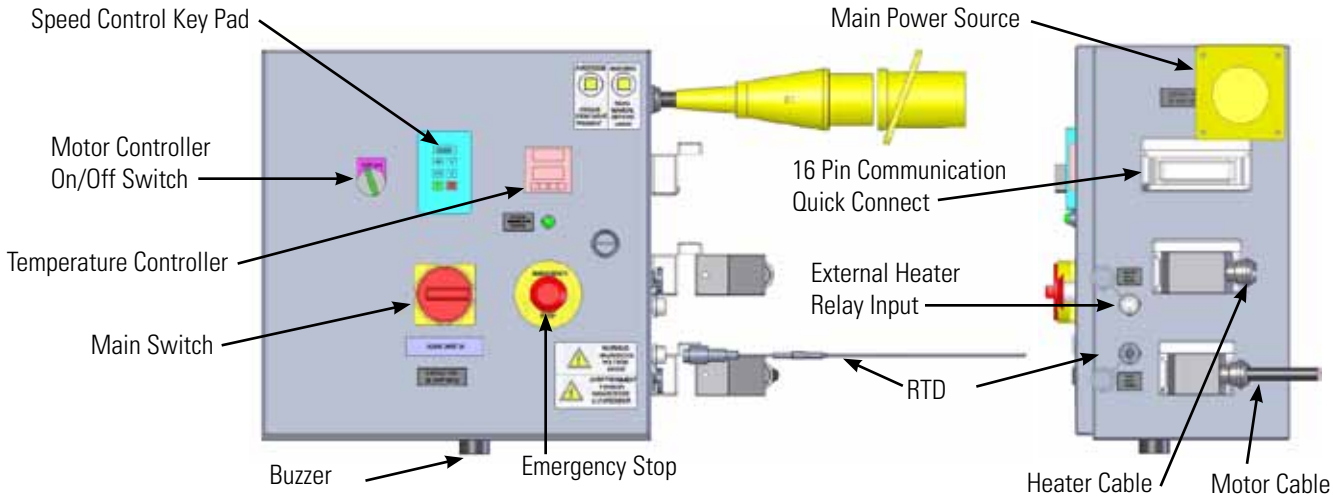
Reactor Geometry	Rated Liquid Working Volume	(50 liter)
	Minimum Liquid Working Volume	(25 liter)
	Total Reactor Volume	(65.5 liter)
	BPC Chamber Diameter	13.75" (34.9 cm)
	BPC Chamber Shoulder Height	31.5" (80 cm)
	Liquid Height @ Rated Working Volume	20.5" (52.1 cm)
	Fluid Geometry @ Working Volume (height/diameter) Ratio	1.5
	Overall Reactor Geometry (height/diameter) Ratio	1.9
	Tank Baffles	no
Impeller	Impeller (quantity X blade count)	1 X 3
	Impeller Scaling (impeller diameter/tank diameter)	1/3
	Impeller Blade Pitch (angle)	45°
	Impeller Diameter	4.63" (11.75 cm)
	Impeller - Calculated Power Number (N)	2.1
Agitation Parameters	Maximum Mixing Rate (revolutions per minute)	30-200 rpm
	Nominal Agitation Rating - Power/Volume Ratio	0.1 hp/1000 gal (19.7 W/1000 liter)
	Nominal Agitation (revolutions per minute)	169 rpm
	Nominal Tip Speed	204.6 ft/min (103.9 cm/s)
	Counterclockwise Mixing Flow Direction	down-pumping
	Agitation Shaft Resolved Angle	19.6°
	Agitation Shaft Centerline Offset	0.75" (1.9 cm)
	Overall Drive Shaft Length	30" (76.2 cm)
	Operational Drive Shaft Length	23" (58.4cm)
	Drive Shaft Diameter	0.5" (1.27cm)
	Drive Shaft Poly-Sheath Outside Diameter	1" (2.54 cm)
	Impeller Clearance from Tank Bottom	4.63" (11.75 cm)
Motor	Agitation Motor Drive (type, voltage, phase)	Induction, 208 VAC, three
	Motor Power Rating	0.25 hp (186.4 kW)
	Motor Torque Rating	82 in-lbs (9.5 Nm)
	Gear Reduction	10:1
	Programmable VFD, Remote Panel Interface, Power Fault Auto-Restart	standard
	Motor Communication Methods (for external controller)	0-10V, 4-20 mA, ModBus
Temp Control	Programmable PID Temperature Controller	standard
	RTD or Thermocouple, 1/8" (3.18 mm) OD	RTD: Pt-100 (standard)
	Heater Style	resistive
	Solid State Relay (discrete voltage signal)	24-240V AC/DC
	Heater Power Rating	400 W
	Approximate Liquid Heat-Up Time: (2-37°C)	8 hr
Support Container	Overall Width	25.8" (65.5 cm)
	Overall Length	36.1" (91.7 cm)
	Overall Height	52.8" (134 cm)
	Dry Skid Weight (mass)	160 lbs (72.7 kg)
	Wet Skid Weight—Rated Working Volume (mass)	270 lbs (122.7 kg)
General	Electrical Power Supply Requirement (voltage, phase, amp)	120/240 VAC, single, 20/10 A
	Operating Temperature (with heater)	Ambient to 40 +/- 0.1 °C (104 +/- 0.2 °F)
	Validated System Reliability (minimum)	0.9 @ 90%

3.1.3 50 L Hardware Specifications Water Jacket

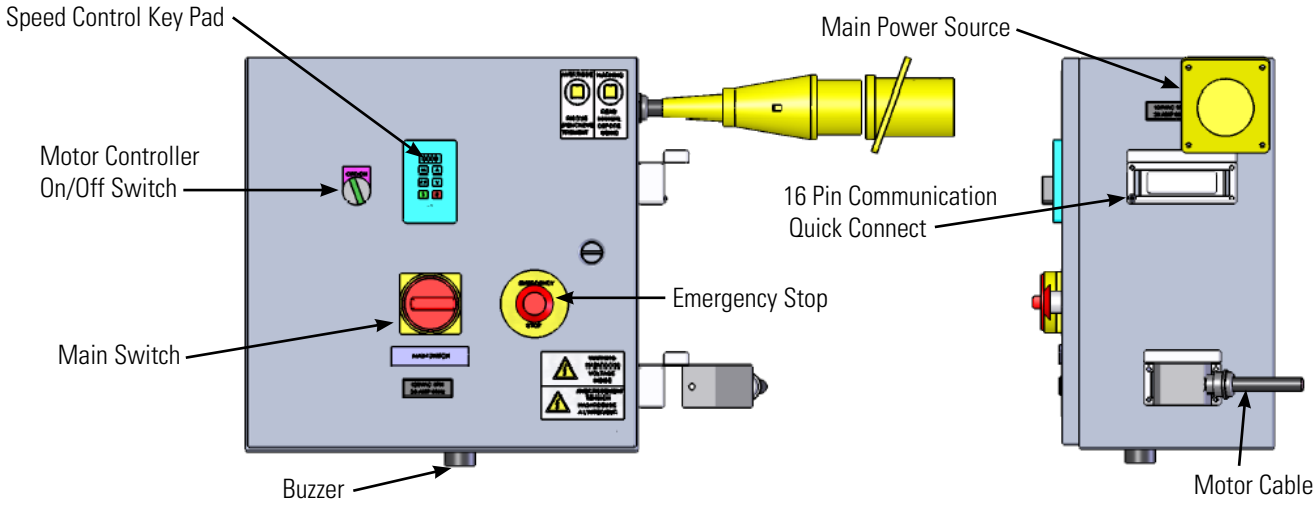
Reactor Geometry	Rated Liquid Working Volume	(50 liter)
	Minimum Liquid Working Volume	(25 liter)
	Total Reactor Volume	(65.5 liter)
	BPC Chamber Diameter	13.75" (34.9 cm)
	BPC Chamber Shoulder Height	31.5" (80 cm)
	Liquid Height @ Rated Working Volume	20.5" (52.1 cm)
	Fluid Geometry @ Working Volume (height/diameter) Ratio	1.5
	Overall Reactor Geometry (height/diameter) Ratio	1.9
	Tank Baffles	no
Impeller	Impeller (quantity X blade count)	1 X 3
	Impeller Scaling (impeller diameter/tank diameter)	1/3
	Impeller Blade Pitch (angle)	45°
	Impeller Diameter	4.63" (11.75 cm)
	Impeller - Calculated Power Number (N)	2.1
Agitation Parameters	Maximum Mixing Rate (revolutions per minute)	30-200 rpm
	Nominal Agitation Rating - Power/Volume Ratio	0.1 hp/1000 gal (19.7 W/1000 liter)
	Nominal Agitation (revolutions per minute)	169 rpm
	Nominal Tip Speed	204.6 ft/min (103.9 cm/s)
	Counterclockwise Mixing Flow Direction	down-pumping
	Agitation Shaft Resolved Angle	19.6°
	Agitation Shaft Centerline Offset	0.75" (1.9 cm)
	Overall Drive Shaft Length	30" (76.2 cm)
	Operational Drive Shaft Length	23" (58.4cm)
	Drive Shaft Diameter	0.5" (1.27cm)
	Drive Shaft Poly-Sheath Outside Diameter	1" (2.54 cm)
	Impeller Clearance from Tank Bottom	4.63" (11.75 cm)
Motor	Agitation Motor Drive (type, voltage, phase)	Induction, 208 VAC, three
	Motor Power Rating	0.25 hp (186.4 kW)
	Motor Torque Rating	82 in-lbs (9.5 Nm)
	Gear Reduction	10:1
	Programmable VFD, Remote Panel Interface, Power Fault Auto-Restart	standard
	Motor Communication Methods (for external controller)	0-10V, 4-20 mA, ModBus
Temp Control	Jacket type	Low profile Stainless Steel Laser Dimpled Jacket with Exterior Insulation Shield
	Jacket area: full/half volume (ft^2)	3.5/1.3
	Jacket Volume (L)	0.30 liters
	Jacket Flow Rate at 50 psi	6.75 liters/min
	RTD or Thermocouple, 1/8" (3.18 mm) OD	RTD: Pt-100 (standard)
	Process Connection	3/4" MNPT nipple with Hansen quick connect check valves
	Nominal heating/cooling load (W)	500
	Nominal heating/cooling time [5-37C] (hr)	3.8
Support Container	Overall Width	23" (58.4 cm)
	Overall Length	34" (86.4 cm)
	Overall Height	52.5" (133.4 cm)
	Dry Skid Weight (mass)	285 lbs (129.3 kg)
	Wet Skid Weight—Rated Working Volume (mass)	395 lbs (179.2 kg)
General	Electrical Power Supply Requirement (voltage, phase, amp)	120/240 VAC, single, 10 A
	Operating Temperature (with heater)	Ambient to 40 +/- 0.1 °C (104 +/- 0.2 °F)
	Validated System Reliability (minimum)	0.9 @ 90%

3.1.4 50 L Control Panel Layout

50 L Control Panel Electric Resistive Heater



50 L Control Panel Water Jacket



3.2 100 L Single-Use Bioreactor

Data Sheet 028 Rev 4

Thermo Scientific HyClone Single-Use Bioreactor (S.U.B.) 100 L

The Thermo Scientific HyClone Single-Use Bioreactor (S.U.B.) is the leading single-use alternative to conventional stirred tank bioreactors for animal and insect cell culture. The current range includes units with maximum working volumes of 50, 100, 250, 500, 1000 and 2000 L. The S.U.B. is now available with new optimized standard BioProcess Containers with improved dual sparge capability. Open pipe and frit sparging systems are now included to provide a wider range of operating conditions.

Overview:

The Thermo Scientific HyClone S.U.B. provides all the advantages of single-use bioprocessing without having to buy a complete new bioreactor system. The critical design parameters of the S.U.B. such as height to diameter ratios, mixer design and location and typical control system interfaces have been maintained.

The S.U.B. BioProcess Container™ (BPC®) is supplied sterilized by irradiation and therefore does not require any facility hook-ups for sterilization or cleaning. A key element to the single-use design is the plastic (polyethylene) impeller with a bearing/seal assembly linked to an external mixer drive.

100 L Water Jacket S.U.B.

This document covers S.U.B. systems with a maximum working volume of 100 L and the new optimized standard S.U.B.s with dual sparge capability which provide a wider range of k_La values, better pH control and lower foaming than the original disk sparger.

The S.U.B. system consists of the following components:

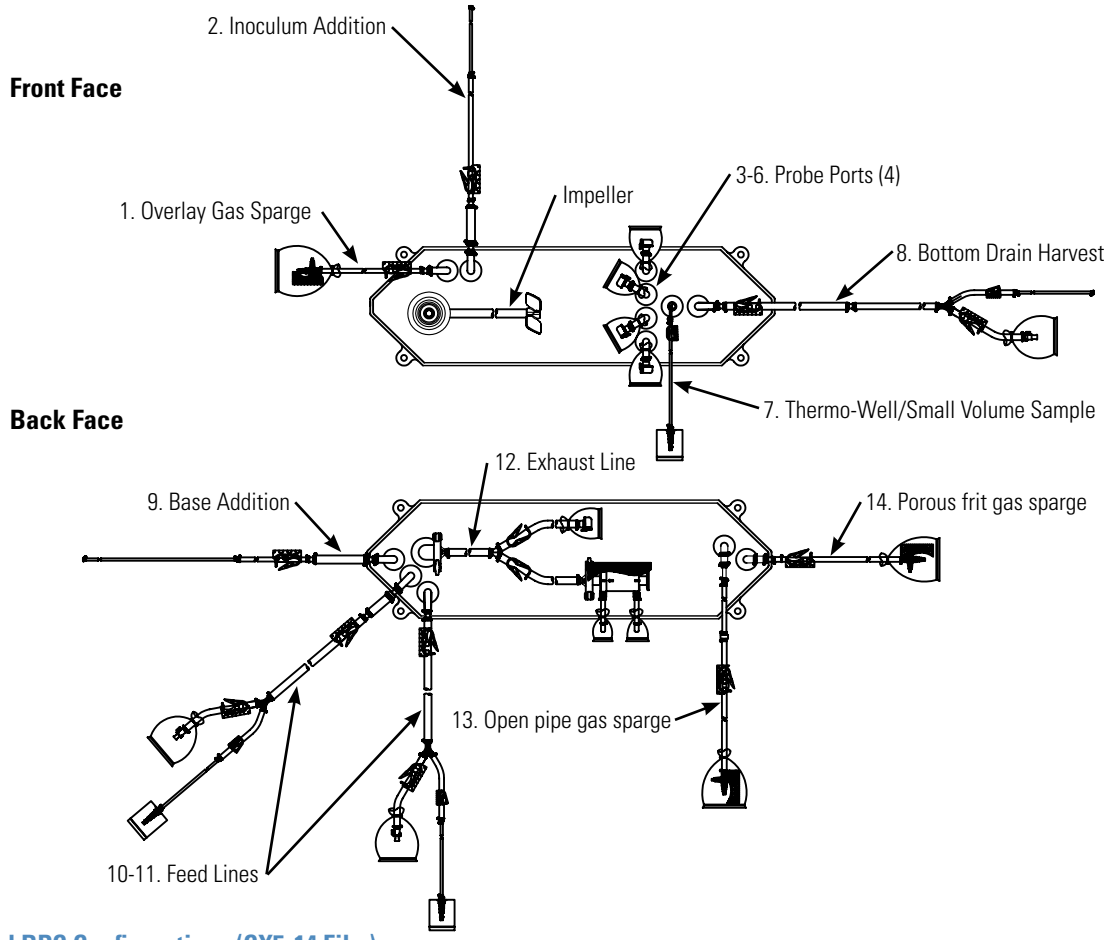
1. Outer Support Container—with a mixer drive complete with control unit and an electrical heater or water jacket.
2. Single-Use Bioreactor BPC—complete with agitator assembly, sparger, vent filter inlet and outlet ports, plus ports for integration of sensor probes and line sets. The S.U.B. BPC is supplied sterile and ready-to-use.
3. Drive Shaft—inserted into the S.U.B. BPC through the mixing drive motor and locked into the disposable agitator assembly.
4. Process Controls—temperature (not on water jacket) and agitation control are integrated into the S.U.B., but additional pH or dissolved oxygen (DO) controls must be supplied by the user.

Item	100 L Electric Resistive Heater	100 L Water Jacket
Rated Liquid Working Volume	100 L	
Minimum Liquid Working Volume	50 L	
Total Reactor Volume (Liquid & Gas)	120 L	
BPC Chamber Diameter	17.25" (43.8 cm)	
BPC Chamber Shoulder Height	37.5" (95.3 cm)	
Liquid Height @ Rated Working Volume	26" (66 cm)	
Overall Reactor Geometry (height/diameter ratio)	1.9:1	
Fluid Geometry @ Working Volume (height/diameter ratio)	1.5:1	
Impeller (quantity x blade count)	1 x 3	
Impeller Diameter	5.75" (14.6 cm)	
pH & DO Probe— Autoclavable Type (Applisens, Broadley James, Metler Toledo)	12 mm diameter x 215-235 mm insertion length x 13.5 PG thread	
Hold-Up Volume	< 0.5 L	
Electrical Power Supply Requirement (voltage, phase, amp)	120/240 VAC, single, 20/10 A	
Overall Width	29.5" (74.93 cm)	
Overall Length	42.0" (106.68 cm)	
Overall Height	56.11" (142.52 cm)	
S.U.B. Recommended Operating Parameters		
Operating Temperature Range	Ambient to 40 +/- 0.1°C (104 +/- 0.2°F)	
Motor Speed	30-200 rpm	
Volume Range	50-100	
Maximum Bag Pressure	0.5 psi (0.03 bar)	
Continuous Operating Time	21 days*	

*Mixing time at nominal volume only.

Standard BPC Configurations (SH30774.02)

For use with tubing welder and CPC Quick Connect



Standard BPC Configurations (CX5-14 Film)

For use with tubing welder and CPC Quick Connect

Line	Description	Tubing Set (ID X OD X Length)	End Treatment
1	Overlay Gas Sparge	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex® X 6" (15 cm)	Hydrophobic vent filter with Emflon® II
2	Inoculum Addition	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 60" (152 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm)	Plugged
3-6	Probe Ports (4)	1/2" (12.7 mm) Tube ports	Pall® Kleenpak™ aseptic connectors—KPCHT Series (Female)
7	Thermo-Well/ Small Volume Sample	Thermo-Well Adapter for 1/4" (6.4 mm) Diameter. 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 18" (46 cm)	SterilEnz® Pouch with injection site assembly
8	Bottom Drain Harvest	1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 60" (152 cm) reduced to 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 12" (30 cm) splits to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 12" 30 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm) and 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 12" (30 cm)	Plugged 3/8" MPC Insert
9	Base Addition	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 6" (15 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 60" (152 cm)	Plugged
10-11	Feed Lines	3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 60" (152 cm) splits to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 12" (30 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm) and 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 12" (30 cm)	SterilEnz Pouch with injection site assembly 3/8" MPC Body
12	Exhaust Line	1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 6" (15 cm) splits to 1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 6" (15 cm) and 1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 10" (25 cm)	Pall Kleenpak aseptic connector—KPCHT Series (Female) Pall Kleenpak 0.2 Micron Exhaust Vent Filter
13	Open Pipe Gas Sparge	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 3" (8 cm) reduced to Check Valve and 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 48" (122 cm)	Hydrophobic vent filter with Emflon II
14	Porous frit gas sparge 12 mm dia (25 µm pores)	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 6" (15 cm) reduced to Check Valve and 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 48" (122 cm)	Hydrophobic vent filter with Emflon II

Ordering Information for Standard BPC Products

Custom BPC Options:

Category	Options/Capability	Remarks
Tubing Type	C Flex, platinum cured silicone, PVC, Pharmed®, PharmaPure®	More information in selection guide of BPC catalog
Tubing Size	Specific lengths of 1/8" ID to 1" ID	ID limitations due to port size
Connectors	Luers, CPC Quick Connects, SIP connectors, Triclamp, Kleenpak, Lynx®, SmartSite®, Clave®, Lynx steam thru, CPC Steam Thru, Gore steam valve, Gore Mini TC, BioQuate (GE), PAW SterilEnz®, end plug, etc.	Refer to selection guide in BPC catalog for further information by connection type. **Note:** Only option for probe port connections is Kleenpak.
Kleenpak (i.e., probe) ports	Additional ports: second row of 4 for 50 L to 250 L S.U.Bs.; second row of 5 for 500 L and 1000 L S.U.B.s	
Disposable sensors	Pressure sensor: Pendotech for 50 L to 250 L S.U.B. (comes standard on 500 L and 1000 L) DO – Finesse DO and pH – PreSens Availability of various other disposable sensors currently pending.	
Addition of ports/lines (other than 2nd row of probe ports)	Limited engineer-to-order customization possible such as additional media lines and vent filter lines. Requires economic justification.	Dependent on location in bag and compatibility with hardware
Port sizes	Limited customization possible as engineer-to-order with justification.	Dependent on location in bag and fit with hardware (e.g., 1" ID port on harvest line)
Re-arrangement of lines on existing ports	Limited customization possible, e.g., moving sample/tempwell port to a probe tube port, or swapping overlay inlet line with supplement line.	Dependent on location in bag and fit with hardware
Sparger	Dual sparger (open pipe plus porous frit) standard. Can do an engineer-to-order for one or the other alone. Make-to-order bags will be built around standard dual sparger chamber.	
Dip tube lines	Limited customization possible. Suggested use through 1" port, so this is engineer-to-order. Otherwise must use ferrule approach.	Length cannot interfere with impeller and shaft. Typical is 10" or shorter.
Overlay and Sparge Line Filters	Can use disposable (capsule) filter other than standard hydrophobic vent filter with Emflon II.	
Vent Filters	Standard is Pall Kleenpak 0.2 micron exhaust vent filter.	**Note:** Vent filter heater configuration restricts options
Vent Filter Tubing Length	Extended filter height above the S.U.B. bag is make-to-order.	Must be compatible with a vent filter bracket option
Filters on Media and Supplement Inlets	Choice of filters for inlets used to sterile filter incoming media or supplements.	

Please Note: Not all options are available for all ports. No customization of port type and location, chamber dimensions or mixing assembly is possible. For additional information, please see the Selection Guides in the S.U.B. BPC Catalog.

Presentation (as dry BPC systems):

Outer Packaging	Supplied 'flat-packed' Two polyethylene outer layers
Label	Description Product code Lot number Expiry date on outer packaging and shipping container
Sterilization	Irradiation (25 to 38 kGy) inside outer packaging
Shipping Container	Durable cardboard carton
Documentation	Certificate of Analysis provided with each lot for each delivery

Hardware Standard Products

Electric Resistive Heater:

Part Number	Description	
SV50197.01	100 L S.U.B., US version (120 VAC, Single Phase)	Includes: 304 stainless steel outer support container with swivel caster platform, variable speed agitation controller, motor, drive assembly with shaft, PID temperature controller, RTD sensor, integrated resistive heating element, probe shelf, and standard tool set
SV50197.02	100 L S.U.B., EU version (240 VAC, Single Phase)	

Water Jacket:

Part Number	Description	
SV50197.03	100 L S.U.B., US version (120 VAC, Single Phase)	Includes: 304 stainless steel outer support container with swivel caster platform, variable speed agitation controller, motor, drive assembly with shaft, RTD sensor, integrated water jacket, probe shelf, and standard tool set
SV50197.04	100 L S.U.B., EU version (240 VAC, Single Phase)	

Custom Options

Custom Hardware Options

For stainless steel capabilities, please contact your sales representative for HyClone products for more information.

Accessories

Part Number	Description	
SH30720.01	Bioreactor Probe Assembly (non-sterile)	Used to package the pH and DO probes (not supplied) for sterilization and to aseptically connect them to the S.U.B. BPC. See Figure 1.
SV20664.01	Heavy Duty Tubing Clamp	Reusable tubing clamp used on probe ports when connecting probe assemblies.
SV20664.02	Heavy Duty Tubing Clamp (4 pack of SV20664.01)	
SV20664.03	Heavy Duty Tubing Clamp (10 pack of SV20664.01)	
SV20750.01	S.U.B. Temperature/Sample Port	Used for RTD calibration/validation.
SV50177.01	Autoclave Tray for Probe Kits (stainless steel)	Support tray which allows the probes to be safely autoclaved. See Figure 2.
SH30845.01	Sterile Sampling Manifold with luer lock (individual)	Available for aseptic luer connection or weld onto the sample line to take sample sets.
SH30845.02	Sterile Sampling Manifold with luer lock (10 pack)	
SV50177.65	Frit Sparge Line Support	Recommended to maintain the frit sparge in a vertical position.
SV50177.16	Elevated Filter Bracket	Needed to support an elevated vent filter.

Figure 1
Bioreactor Probe Assembly

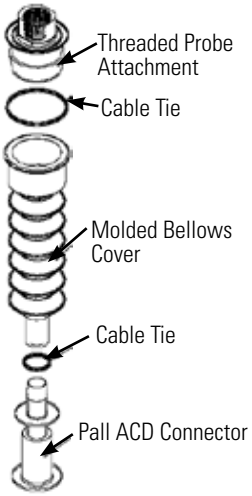
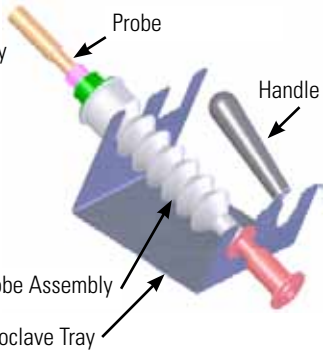


Figure 2
Autoclave Tray for Probe Kits

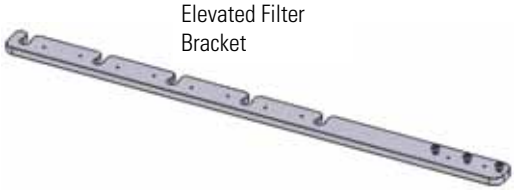


Additional information on autoclave tray:

- Fabricated from stainless steel
- Plastic carry handle for easy transport right out of the autoclave
- Positions probes on 15% incline for greater probe/membrane longevity
- Will restrain probe bellows from collapsing during sterilization
- Probe holder accommodates two probes

Figure 4
Frit Sparge Line Support

Figure 3
Elevated Filter Bracket



Single-Use Bioreactor (S.U.B.) First Time Operator—Recommended Parts List

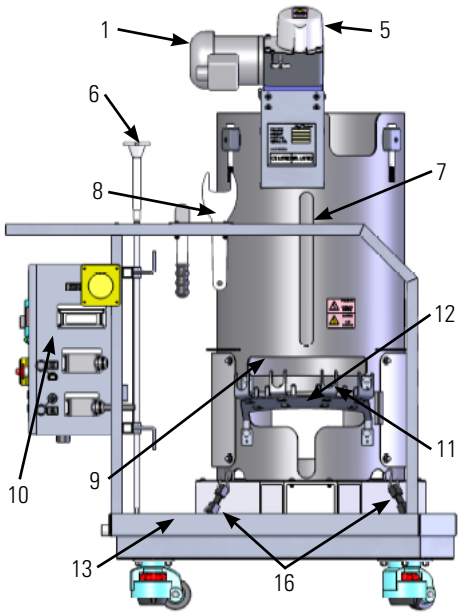
Parts Available From HyClone (consumables sufficient for three complete cell culture runs)		
Description	**Part Number**	**Quantity**
SV50197 (100 L)	S.U.B. Hardware System (standard)	1
SH30774.02	S.U.B. BPC (standard)	3
SH30720.01	Bioreactor Probe Assembly (non-sterile for use in autoclave)	12
SV20664.03	Heavy Duty Tubing Clamp (10 pack)	1
SV50177.01	Autoclave Tray for Autoclaving Probe Kits	2
SV20750.01	S.U.B. Temperature Port (used to verify RTD calibration)	1
SH30845.02	Sterile Sampling Manifold with Luer Locks (10 pack)	3
Auxiliary Components Supporting The Single-Use Bioreactor		
Description	**Purpose**	**Quantity**
Bioreactor control system	Necessary for regulation of gas pressure and flow rate control for DO and pH set points	1
DO probe	Autoclavable Probe (13 mm X 13.5 PG thread w/ 195-235 mm insertion length)	1
pH probe	Autoclavable Probe (13 mm X 13.5 PG thread w/ 195-235 mm insertion length)	1
Sterile/Aseptic Connection Method	Tubing Welder (Terumo or Wave), Steam In Place (SIP) Sterilizer, or Laminar Flow Hood	1
Peristaltic Pump	Used for fluid transfer between line sets and containers	1
Temperature Control Unit (TCU)	Necessary for water jacket temperature control (not provided by Thermo Scientific)	1

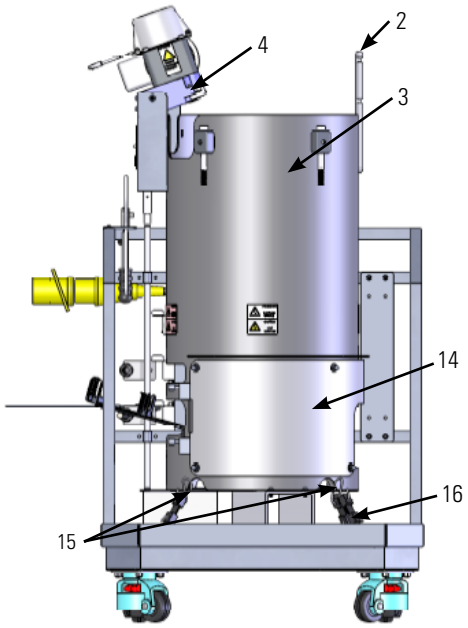
Hardware Features

100 L with Resistive Heater:

The stainless steel outer support container contains the following features:

1. Mixer motor
2. Exhaust vent filter holder
3. Stainless steel (304) outer support container
4. Bearing port receiver with clamp
5. Mixing assembly with shield
6. Drive shaft
7. Liquid sight window
8. Standard tool set
9. Probe access window
10. Control panel
11. Probe holder
12. Probe shelf
13. Platform with swivel casters and leveling pads
14. Resistive heater w/ heat shield
15. Bottom cut outs for BPC alignment
16. Stretch hooks



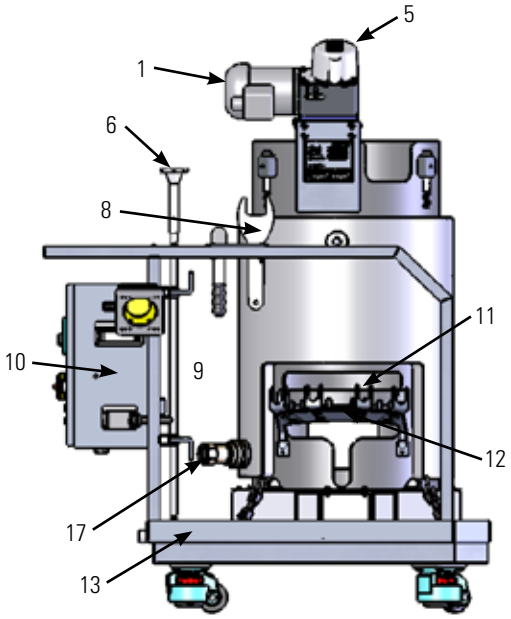


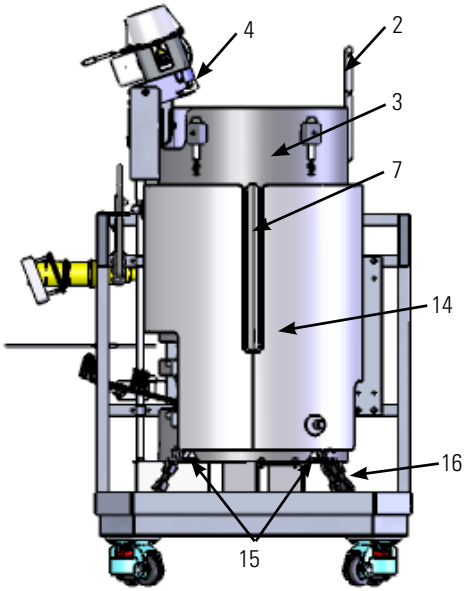
Hardware Features

100 L with Water Jacket:

The stainless steel outer support container contains the following features:

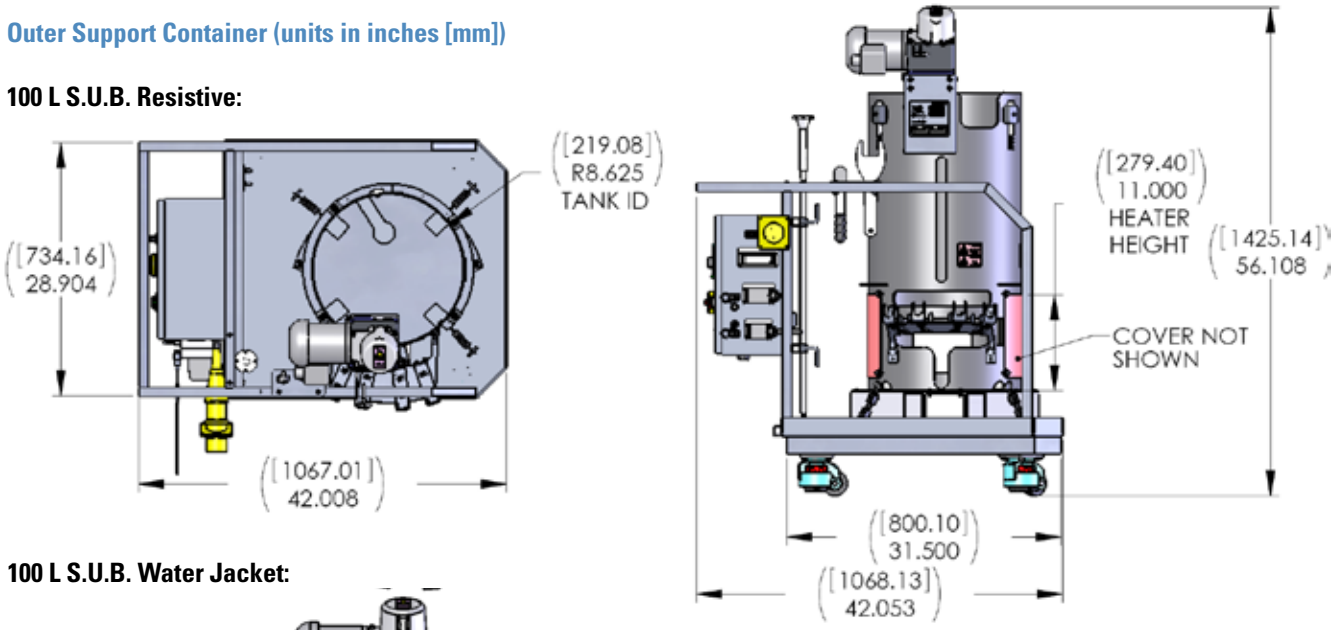
1. Mixer motor
2. Exhaust vent filter holder
3. Stainless steel (304) outer support container
4. Bearing port receiver with clamp
5. Mixing assembly with shield
6. Drive shaft
7. Liquid sight window
8. Standard tool set
9. Probe access window
10. Control panel
11. Probe holder
12. Probe shelf
13. Platform with swivel casters and leveling pads
14. Laser Dimple Water Jacket
15. Bottom cut outs for BPC alignment
16. Stretch hooks
17. Jacket quick connect couplings



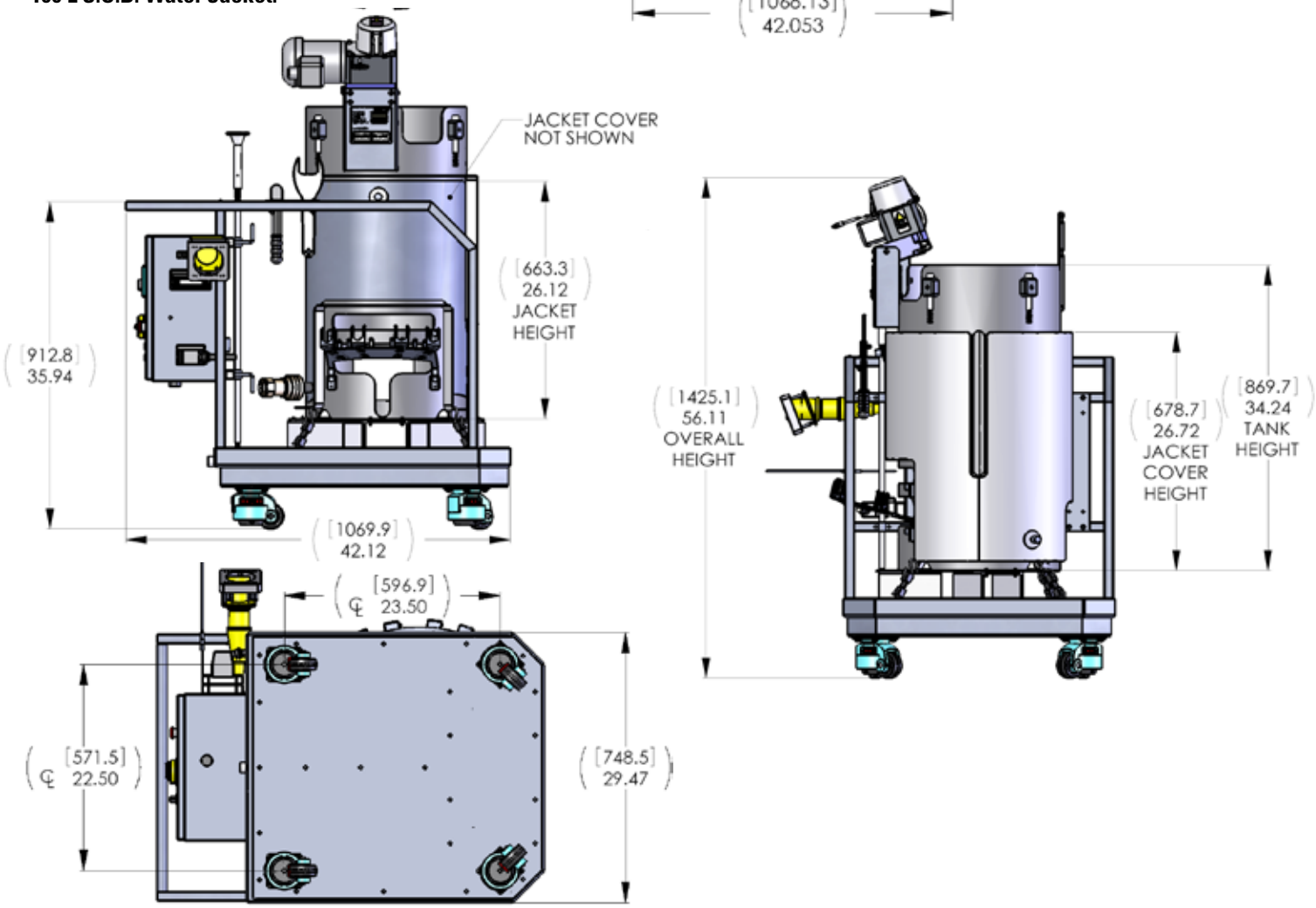


Outer Support Container (units in inches [mm])

100 L S.U.B. Resistive:



100 L S.U.B. Water Jacket:



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Thermo SCIENTIFIC

3.2.2 100 L Hardware Specifications Electric Resistive Heater

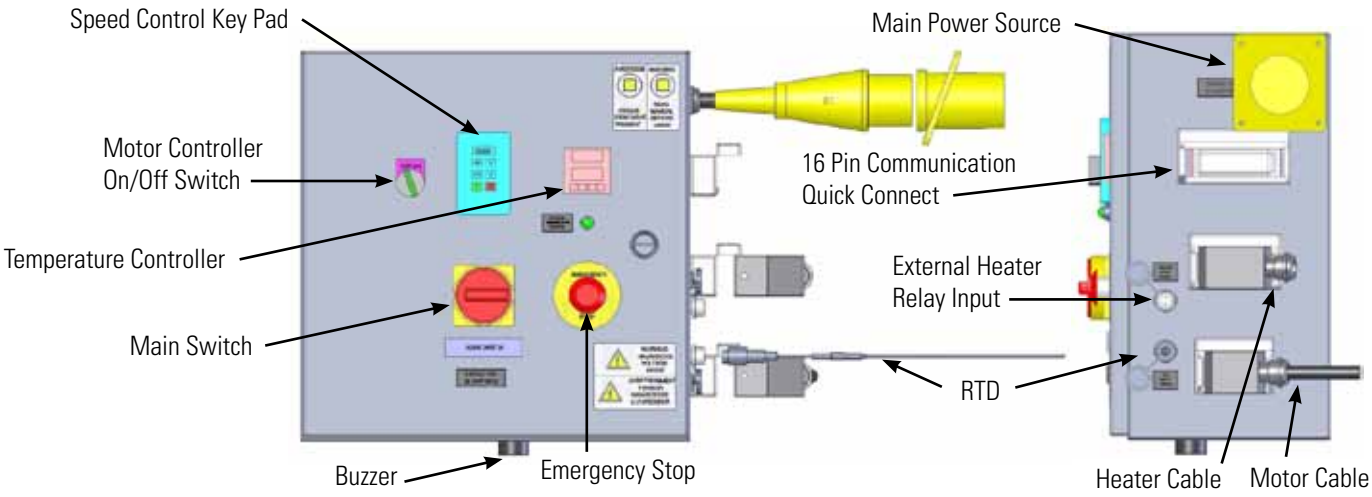
Reactor Geometry	Rated Liquid Working Volume	(100 liter)
	Minimum Liquid Working Volume	(50 liter)
	Total Reactor Volume	(131 liter)
	BPC Chamber Diameter	17.25" (43.8 cm)
	BPC Chamber Shoulder Height	37.5" (95.3 cm)
	Liquid Height @ Rated Working Volume	26" (71.1 cm)
	Fluid Geometry @ Working Volume (height/diameter) Ratio	1.5
	Overall Reactor Geometry (height/diameter) Ratio	1.9
	Tank Baffles	no
Impeller	Impeller (quantity X blade count)	1 X 3
	Impeller Scaling (impeller diameter/tank diameter)	1/3
	Impeller Blade Pitch (angle)	45°
	Impeller Diameter	5.75" (14.6 cm)
	Impeller - Calculated Power Number (N)	2.1
Agitation Parameters	Maximum Mixing Rate (revolutions per minute)	30-200 rpm
	Nominal Agitation Rating - Power/Volume Ratio	0.1 hp/1000 gal (19.7 W/1000 liter)
	Nominal Agitation (revolutions per minute)	145.5 rpm
	Nominal Tip Speed	218.0 ft/min (110.7 cm/s)
	Counterclockwise Mixing Flow Direction	down-pumping
	Agitation Shaft Resolved Angle	19.6°
	Agitation Shaft Centerline Offset	1.00" (2.54 cm)
	Overall Drive Shaft Length	35" (88.9 cm)
	Operational Drive Shaft Length	29" (73.6 cm)
	Drive Shaft Diameter	0.5" (1.27cm)
	Drive Shaft Poly-Sheath Outside Diameter	1" (2.54 cm)
	Impeller Clearance from Tank Bottom	5.75" (14.6 cm)
Motor	Agitation Motor Drive (type, voltage, phase)	Induction, 208 VAC, three
	Motor Power Rating	0.25 hp (186.4 kW)
	Motor Torque Rating	82 in-lbs (9.5 Nm)
	Gear Reduction	10:1
	Programmable VFD, Remote Panel Interface, Power Fault Auto-Restart	standard
	Motor Communication Methods (for external controller)	0-10V, 4-20 mA, ModBus
Temp Control	Programmable PID Temperature Controller	standard
	RTD or Thermocouple, 1/8" (3.18 mm) OD	RTD: Pt-100 (standard)
	Heater Style	resistive
	Solid State Relay (discrete voltage signal)	24-240V AC/DC
	Heater Power Rating	600 W
	Approximate Liquid Heat-Up Time: (2-37°C)	8 hr
Support Container	Overall Width	29.5" (74.9 cm)
	Overall Length	42" (106.7cm)
	Overall Height	56" (142.2 cm)
	Dry Skid Weight (mass)	121 lbs (54.9 kg)
	Wet Skid Weight—Rated Working Volume (mass)	341 lbs (154.7 kg)
General	Electrical Power Supply Requirement (voltage, phase, amp)	120/240 VAC, single, 20/10 A
	Operating Temperature (with heater)	Ambient to 40 +/- 0.1 °C (104 +/- 0.2 °F)
	Validated System Reliability (minimum)	0.9 @ 90%

3.2.3 100 L Hardware Specifications Water Jacket

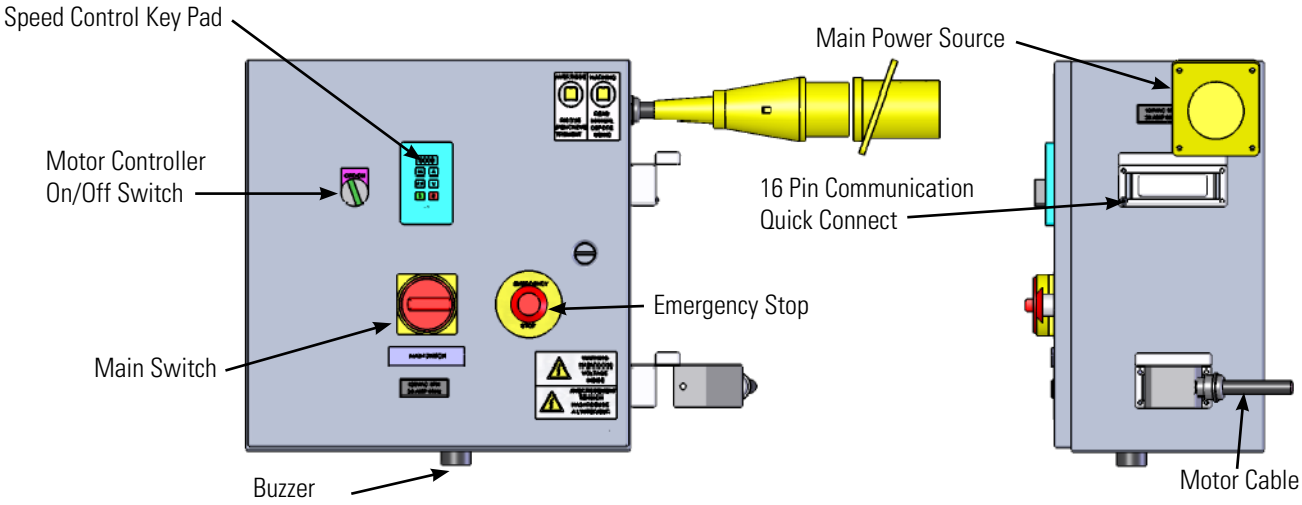
Reactor Geometry	Rated Liquid Working Volume	(100 liter)
	Minimum Liquid Working Volume	(50 liter)
	Total Reactor Volume	(131 liter)
	BPC Chamber Diameter	17.25" (43.8 cm)
	BPC Chamber Shoulder Height	37.5" (95.3 cm)
	Liquid Height @ Rated Working Volume	26" (66.0 cm)
	Fluid Geometry @ Working Volume (height/diameter) Ratio	1.5
	Overall Reactor Geometry (height/diameter) Ratio	1.9
	Tank Baffles	no
Impeller	Impeller (quantity X blade count)	1 X 3
	Impeller Scaling (impeller diameter/tank diameter)	1/3
	Impeller Blade Pitch (angle)	45°
	Impeller Diameter	5.75" (14.6 cm)
	Impeller - Calculated Power Number (N)	2.1
Agitation Parameters	Maximum Mixing Rate (revolutions per minute)	30-200 rpm
	Nominal Agitation Rating - Power/Volume Ratio	0.1 hp/1000 gal (19.7 W/1000 liter)
	Nominal Agitation (revolutions per minute)	145.5 rpm
	Nominal Tip Speed	218.0 ft/min (110.7 cm/s)
	Counterclockwise Mixing Flow Direction	down-pumping
	Agitation Shaft Resolved Angle	19.6°
	Agitation Shaft Centerline Offset	1.00" (2.54 cm)
	Overall Drive Shaft Length	35" (88.9 cm)
	Operational Drive Shaft Length	29" (73.7 cm)
	Drive Shaft Diameter	0.5" (1.27 cm)
	Drive Shaft Poly-Sheath Outside Diameter	1" (2.54 cm)
	Impeller Clearance from Tank Bottom	5.75" (14.6 cm)
Motor	Agitation Motor Drive (type, voltage, phase)	Induction, 208 VAC, three
	Motor Power Rating	0.25 hp (186.4 kW)
	Motor Torque Rating	82 in-lbs (9.5 Nm)
	Gear Reduction	10:1
	Programmable VFD, Remote Panel Interface, Power Fault Auto-Restart	standard
	Motor Communication Methods (for external controller)	0-10V, 4-20 mA, ModBus
Temp Control	Jacket type	Low profile Stainless Steel Laser Dimpled Jacket with Exterior Insulation Shield
	Jacket area: full/half volume (ft^2)	6.5/2.3
	Jacket Volume (L)	0.50 liters
	Jacket Flow Rate at 50 psi	7.75 liters/min
	RTD or Thermocouple, 1/8" (3.18 mm) OD	RTD: Pt-100 (standard)
	Process Connection	3/4" MNPT nipple with Hansen quick connect check valves
	Nominal heating/cooling load (W)	1000
	Nominal heating/cooling time [5-37C] (hr)	4.7
Support Container	Overall Width	29.5" (74.9 cm)
	Overall Length	42" (106.7 cm)
	Overall Height	56" (142.2 cm)
	Dry Skid Weight (mass)	372 lbs (168.7 kg)
	Wet Skid Weight—Rated Working Volume (mass)	592 lbs (268.5 kg)
General	Electrical Power Supply Requirement (voltage, phase, amp)	120/240 VAC, single, 15 A
	Operating Temperature (with heater)	5 to 40 +/- 0.1 °C (104 +/- 0.2 °F)
	Validated System Reliability (minimum)	0.9 @ 90%

3.2.4 100 L Control Panel Layout

100 L Control Panel Electric Resistive Heater



100 L Control Panel Water Jacket



3.3 250 L Single-Use Bioreactor

Data Sheet 029 Rev 5

Thermo Scientific HyClone Single-Use Bioreactor (S.U.B.) 250 L

The Thermo Scientific HyClone Single-Use Bioreactor (S.U.B.) is the leading single-use alternative to conventional stirred tank bioreactors for animal and insect cell culture. The current range includes units with maximum working volumes of 50, 100, 250, 500, 1000 and 2000 L. The S.U.B. is now available with new optimized standard BioProcess Containers with improved dual sparge capability. Open pipe and frit sparging systems are now included to provide a wider range of operating conditions.

Overview:

The HyClone® S.U.B. provides all the advantages of single-use bioprocessing without having to buy a complete new bioreactor system. The critical design parameters of the S.U.B., such as height to diameter ratios, mixer design and location and typical control system interfaces, have been maintained.

The S.U.B. BioProcess Container™ (BPC®) is supplied sterilized by irradiation and therefore does not require any facility hook-ups for sterilization or cleaning. A key element to the single-use design is the plastic (polyethylene) impeller with a bearing/seal assembly linked to an external mixer drive.

250 L Water Jacket S.U.B.

This document covers S.U.B. systems with a maximum working volume of 250 L and the new optimized standard S.U.B.s with dual sparge capability which provide a wider range of k_La values, better pH control and lower foaming than the original disk sparger.

The S.U.B. system consists of the following components:

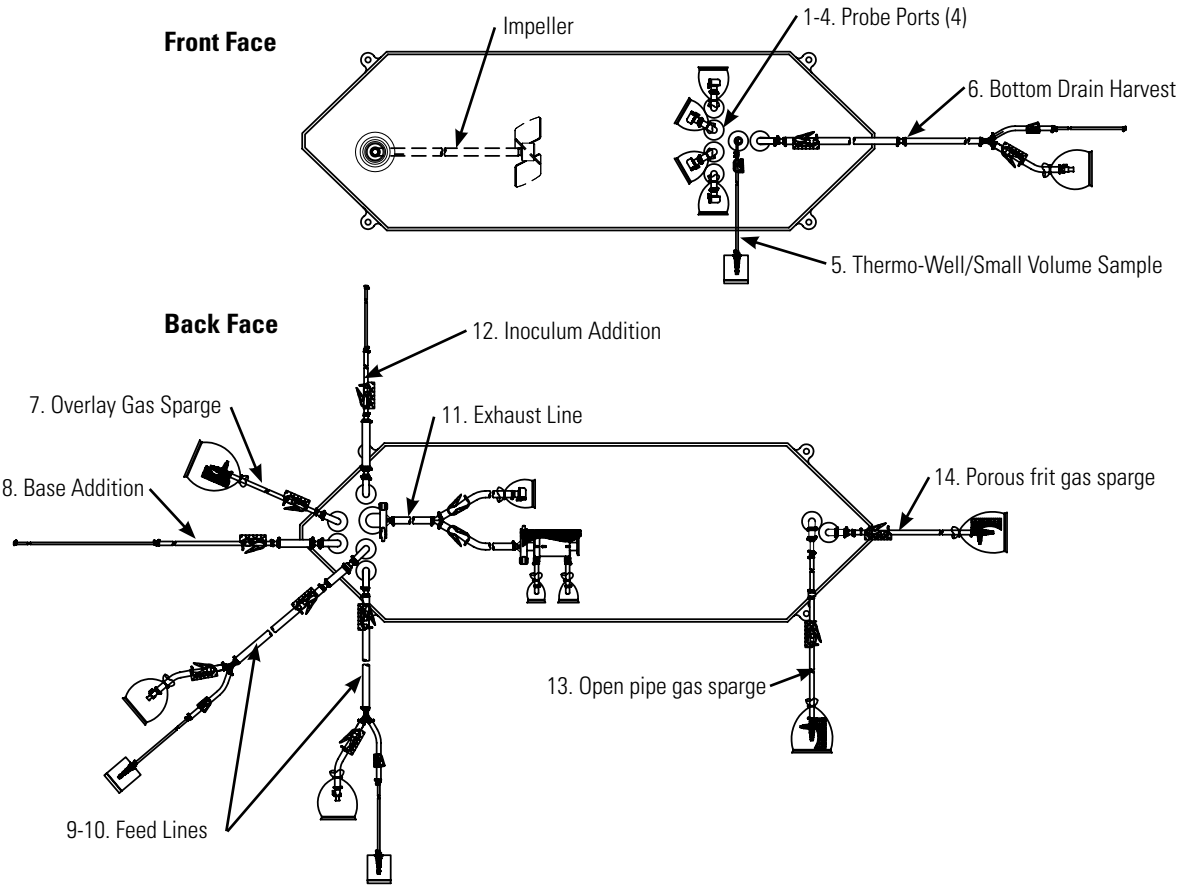
1. Outer Support Container—with a mixer drive complete with control unit and an electrical heater or water jacket.
2. Single-Use Bioreactor BPC—complete with agitator assembly, sparger, vent filter inlet and outlet ports, plus ports for integration of sensor probes and line sets. The S.U.B. BPC is supplied sterile and ready-to-use.
3. Drive Shaft—inserted into the S.U.B. BPC through the mixing drive motor and locked into the disposable agitator assembly.
4. Process Controls—temperature (not on water jacket) and agitation control are integrated into the S.U.B., but additional pH or dissolved oxygen (DO) controls must be supplied by the user.

Item	250 L Electric Resistive Heater	250 L Water Jacket
Rated Liquid Working Volume	250 L	
Minimum Liquid Working Volume	125 L	
Total Reactor Volume (Liquid & Gas)	316 L	
BPC Chamber Diameter	23.5" (59.7 cm)	
BPC Chamber Shoulder Height	45.5" (115.6 cm)	
Liquid Height @ Rated Working Volume	36" (91.4 cm)	
Overall Reactor Geometry (height/diameter ratio)	1.9:1	
Fluid Geometry @ Working Volume (height/diameter ratio)	1.5:1	
Impeller (quantity x blade count)	1 x 3	
Impeller Diameter	7.88" (20 cm)	7.88" (20 cm)
pH & DO Probe— Autoclavable Type (Applisens, Broadley James, Metler Toledo)	12 mm diameter x 215-235 mm insertion length x 13.5 PG thread	
Hold-Up Volume	< 1 L	
Electrical Power Supply Requirement (voltage, phase, amp)	120/240 VAC, single, 20/10 A	120/240 VAC, single, 10 A
Overall Width	26" (66 cm)	
Overall Length	35" (88.9 cm)	
Overall Height	60" (152.4 cm)	
S.U.B. Recommended Operating Parameters		
Operating Temperature Range	Ambient to 40 +/- 0.1°C (104 +/- 0.2°F)	
Motor Speed	30-150 rpm	
Volume Range	125-250 L	
Maximum Bag Pressure	0.5 psi (0.03 bar)	
Continuous Operating Time	21 days*	

*Mixing time at nominal volume only.

Standard BPC Configurations (SH30774.03)

For use with tubing welder and CPC Quick Connect



Standard BPC Configurations (CX5-14 Film)

For use with tubing welder (CPC Quick Connect or Triclamp End Treatments)

Line	Description	Tubing Set (ID X OD X Length)	End Treatment
1-4	Probe Ports (4)	1/2" (12.7 mm) Tube ports	Pall® Kleenpak™ aseptic connectors—KPCHT Series (Female)
5	Thermo-Well/ Small Volume Sample	Thermo-Well Adapter for 1/4" (6.4 mm) Diameter. 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex® X 18" (46 cm)	SterilEnz® Pouch with injection site assembly
6	Bottom Drain Harvest	1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 60" (152 cm) reduced to 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 12" (30 cm) splits to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 12" 30 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm) and 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 12" (30 cm)	Plugged 3/8" MPC Insert
7	Overlay Gas Sparge	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 6" (15 cm)	Hydrophobic vent filter with Emflon® II
8	Base Addition	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 6" (15 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 60" (152 cm)	Plugged
9-10	Feed Lines	3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 60" (152 cm) splits to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 12" (30 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm) and 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 12" (30 cm)	SterilEnz Pouch with injection site assembly 3/8" MPC Body
11	Exhaust Line	1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 6" (15 cm) splits to 1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 6" (15 cm) and 1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 10" (25 cm)	Pall Kleenpak aseptic connector—KPCHT Series (Female) Pall Kleenpak 0.2 Micron Exhaust Vent Filter
12	Inoculum Addition	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 60" (152 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm)	Plugged
13	Open Pipe Gas Sparge	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 3" (8 cm) reduced to Check Valve and 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 48" (122 cm)	Hydrophobic vent filter with Emflon II
14	Porous frit gas sparge 12 mm dia (25 µm pores)	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 6" (15 cm) reduced to Check Valve and 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 48" (122 cm)	Hydrophobic vent filter with Emflon II

Ordering Information for Standard BPC Products

Custom BPC Options:

Category	Options/Capability	Remarks
Tubing Type	C Flex, platinum cured silicone, PVC, Pharmed®, PharmaPure®	More information in selection guide of BPC catalog
Tubing Size	Specific lengths of 1/8" ID to 1" ID	ID limitations due to port size
Connectors	Luers, CPC Quick Connects, SIP connectors, Triclamp, Kleenpak, Lynx®, SmartSite®, Clave®, Lynx steam thru, CPC Steam Thru, Gore steam valve, Gore Mini TC, BioQuate (GE), PAW SterilEnz®, end plug, etc.	Refer to selection guide in BPC catalog for further information by connection type. **Note:** Only option for probe port connections is Kleenpak.
Kleenpak (i.e., probe) ports	Additional ports: second row of 4 for 50 L to 250 L S.U.Bs.; second row of 5 for 500 L and 1000 L S.U.B.s	
Disposable sensors	Pressure sensor: Pendotech for 50 L to 250 L S.U.B. (comes standard on 500 L and 1000 L) DO – Finesse DO and pH – PreSens Availability of various other disposable sensors currently pending.	
Addition of ports/lines (other than 2nd row of probe ports)	Limited engineer-to-order customization possible such as additional media lines and vent filter lines. Requires economic justification.	Dependent on location in bag and compatibility with hardware
Port sizes	Limited customization possible as engineer-to-order with justification.	Dependent on location in bag and fit with hardware (e.g., 1" ID port on harvest line)
Re-arrangement of lines on existing ports	Limited customization possible, e.g., moving sample/tempwell port to a probe tube port, or swapping overlay inlet line with supplement line.	Dependent on location in bag and fit with hardware
Sparger	Dual sparger (open pipe plus porous frit) standard. Can do an engineer-to-order for one or the other alone. Make-to-order bags will be built around standard dual sparger chamber.	
Dip tube lines	Limited customization possible. Suggested use through 1" port, so this is engineer-to-order. Otherwise must use ferrule approach.	Length cannot interfere with impeller and shaft. Typical is 10" or shorter.
Overlay and Sparge Line Filters	Can use disposable (capsule) filter other than standard hydrophobic vent filter with Emflon II.	
Vent Filters	Standard is Pall Kleenpak 0.2 micron exhaust vent filter.	**Note:** Vent filter heater configuration restricts options
Vent Filter Tubing Length	Extended filter height above the S.U.B. bag is make-to-order.	Must be compatible with a vent filter bracket option
Filters on Media and Supplement Inlets	Choice of filters for inlets used to sterile filter incoming media or supplements.	

Please Note: Not all options are available for all ports. No customization of port type and location, chamber dimensions or mixing assembly is possible. For additional information, please see the Selection Guides in the S.U.B. BPC Catalog.

Presentation (as dry BPC systems):

Outer Packaging	Supplied 'flat-packed' Two polyethylene outer layers
Label	Description Product code Lot number Expiry date on outer packaging and shipping container
Sterilization	Irradiation (25 to 38 kGy) inside outer packaging
Shipping Container	Durable cardboard carton
Documentation	Certificate of Analysis provided with each lot for each delivery

Hardware Standard Products

Electric Resistive Heater:

Part Number	Description	
SV50172.01	250 L S.U.B., US version (120 VAC, Single Phase)	Includes: 304 stainless steel outer support container with swivel caster platform, variable speed agitation controller, motor, drive assembly with shaft, PID temperature controller, RTD sensor, integrated resistive heating element, probe shelf and standard tool set
SV50172.02	250 L S.U.B., EU version (240 VAC, Single Phase)	

Water Jacket:

Part Number	Description	
SV50172.03	250 L S.U.B., US version (120 VAC, Single Phase)	Includes: 304 stainless steel outer support container with swivel caster platform, variable speed agitation controller, motor, drive assembly with shaft, RTD sensor, integrated water jacket, probe shelf and standard tool set
SV50172.04	250 L S.U.B., EU version (240 VAC, Single Phase)	

Custom Options

Custom Hardware Options:

For stainless steel capabilities, please contact your sales representative for HyClone products for more information.

Accessories

Part Number	Description	
SH30720.01	Bioreactor Probe Assembly (non-sterile)	Used to package the pH and DO probes (not supplied) for sterilization and to aseptically connect them to the S.U.B. BPC. See Figure 1.
SV20664.01	Heavy Duty Tubing Clamp	Reusable tubing clamp used on probe ports when connecting probe assemblies.
SV20664.02	Heavy Duty Tubing Clamp (4 pack of SV20664.01)	
SV20664.03	Heavy Duty Tubing Clamp (10 pack of SV20664.01)	
SV20750.01	S.U.B. Temperature/Sample Port	Used for RTD calibration/validation.
SV50177.01	Autoclave Tray for Probe Kits (stainless steel)	Support tray which allows the probes to be safely autoclaved. See Figure 2.
SH30845.01	Sterile Sampling Manifold with luer lock (individual)	Available for aseptic luer connection or weld onto the sample line to take sample sets.
SH30845.02	Sterile Sampling Manifold with luer lock (10 pack)	
SV50177.65	Frit Sparge Line Support	Recommended to maintain the frit sparge in a vertical position.
SV50177.16	Elevated Filter Bracket	Needed to support an elevated vent filter.

Figure 1
Bioreactor Probe Assembly

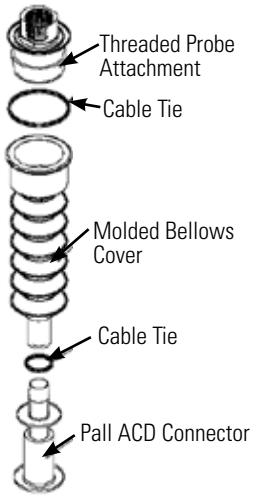
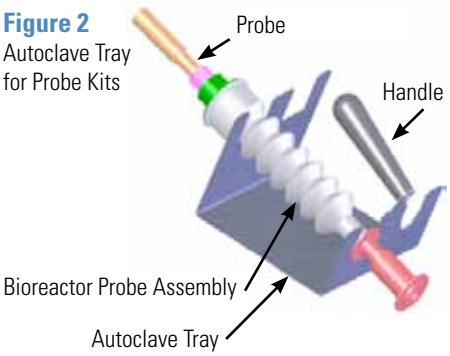


Figure 2
Autoclave Tray for Probe Kits

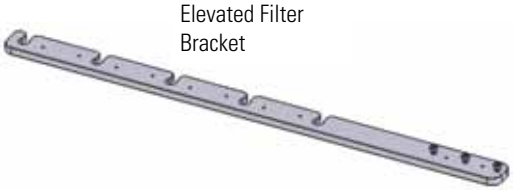


Additional information on autoclave tray:

- Fabricated from stainless steel
- Plastic carry handle for easy transport right out of the autoclave
- Positions probes on 15% incline for greater probe/membrane longevity
- Will restrain probe bellows from collapsing during sterilization
- Probe holder accommodates two probes

Figure 4
Frit Sparge Line Support

Figure 3
Elevated Filter Bracket



Single-Use Bioreactor (S.U.B.) First Time Operator—Recommended Parts List

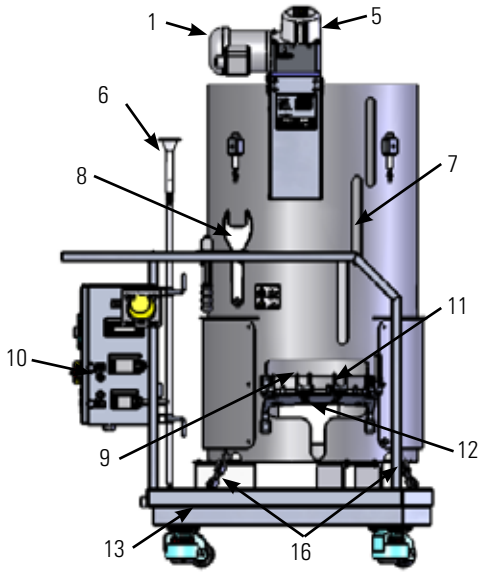
Available Parts (consumables sufficient for three complete cell culture runs)		
Part Number	**Description**	**Quantity**
SV50172 (250 L)	S.U.B. Hardware System (standard)	1
SH30774.03	S.U.B. BPC (standard)	3
SH30720.01	Bioreactor Probe Assembly (non-sterile for use in autoclave)	12
SV20664.03	Heavy Duty Tubing Clamp (10 pack)	1
SV50177.01	Autoclave Tray for Autoclaving Probe Kits	2
SV20750.01	S.U.B. Temperature Port (used to verify RTD calibration)	1
SH30845.02	Sterile Sampling Manifold with Luer Locks (10 pack)	3
Auxiliary Components Supporting The Single-Use Bioreactor		
Description	**Purpose**	**Quantity**
Bioreactor control system	Necessary for regulation of gas pressure and flow rate control for DO and pH set points	1
DO probe	Autoclavable Probe (13 mm X 13.5PG thread w/ 195-235 mm insertion length)	1
pH probe	Autoclavable Probe (13 mm X 13.5PG thread w/ 195-235 mm insertion length)	1
Sterile/Aseptic Connection Method	Tubing Welder (Terumo or Wave), Steam In Place (SIP) Sterilizer, or Laminar Flow Hood	1
Peristaltic Pump	Used for fluid transfer between line sets and containers	1
Temperature Control Unit (TCU)	Necessary for water jacket temperature control (not provided)	1

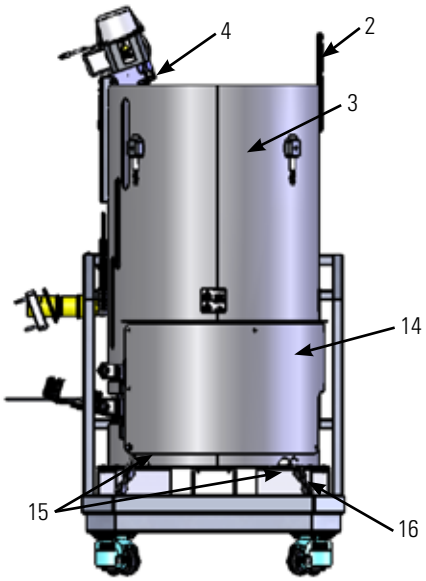
Hardware Features

250 L with Resistive Heater:

The stainless steel outer support container contains the following features:

1. Mixer motor
2. Exhaust vent filter holder
3. Stainless steel (304) outer support container
4. Bearing port receiver with clamp
5. Mixing assembly with shield
6. Drive shaft
7. Liquid sight window
8. Standard tool set
9. Probe access window
10. Control panel
11. Probe holder
12. Probe shelf
13. Platform with swivel casters and leveling pads
14. Resistive heater w/heat shield
15. Bottom cut outs for BPC alignment
16. Stretch hooks



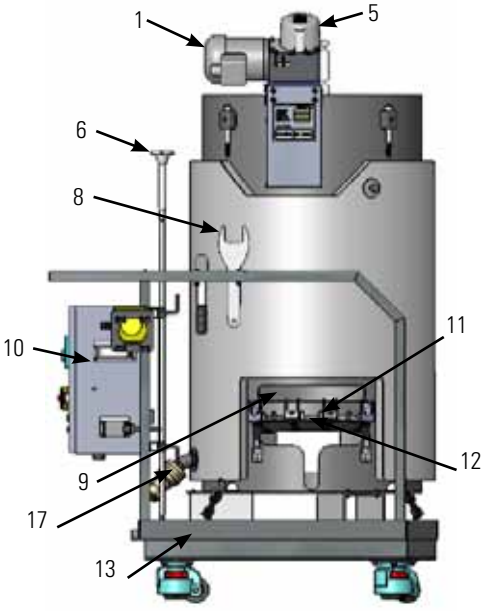


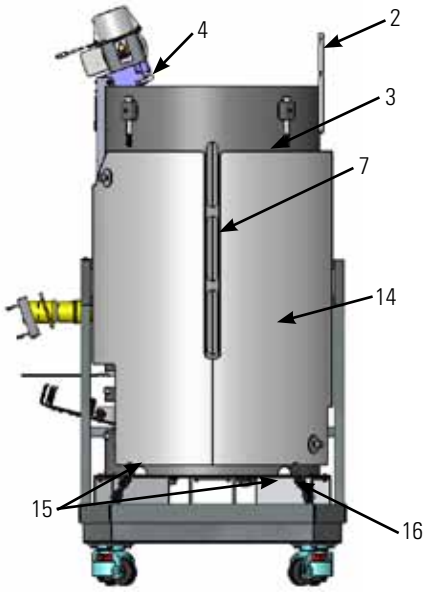
Hardware Features

250 L with Water Jacket:

The stainless steel outer support container contains the following features:

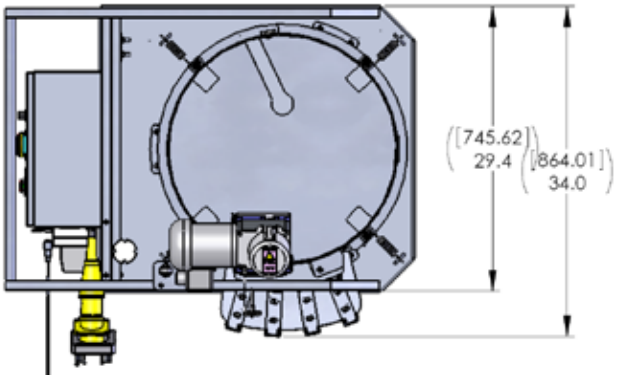
1. Mixer motor
2. Exhaust vent filter holder
3. Stainless steel (304) outer support container
4. Bearing port receiver with clamp
5. Mixing assembly with shield
6. Drive shaft
7. Liquid sight window
8. Standard tool set
9. Probe access window
10. Control panel
11. Probe holder
12. Probe shelf
13. Platform with swivel casters and leveling pads
14. Laser dimple water jacket
15. Bottom cut outs for BPC alignment
16. Stretch hooks
17. Jacket quick connect couplings

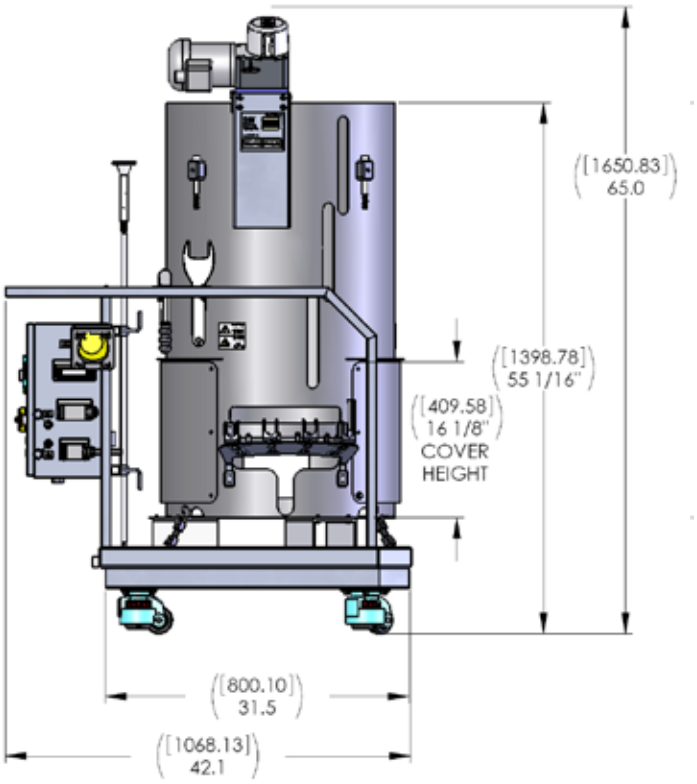




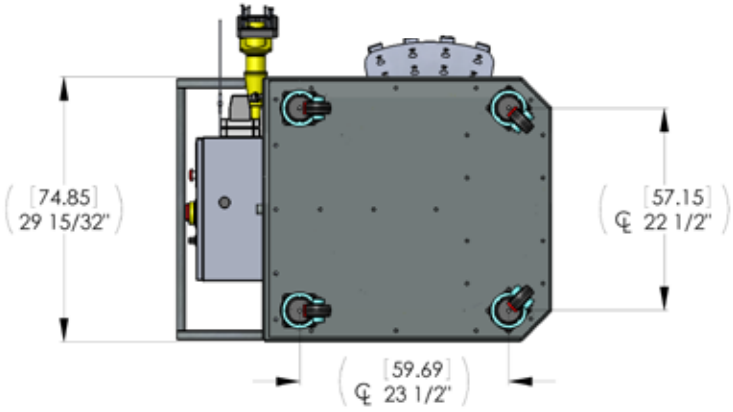
Outer Support Container (units in inches [mm])

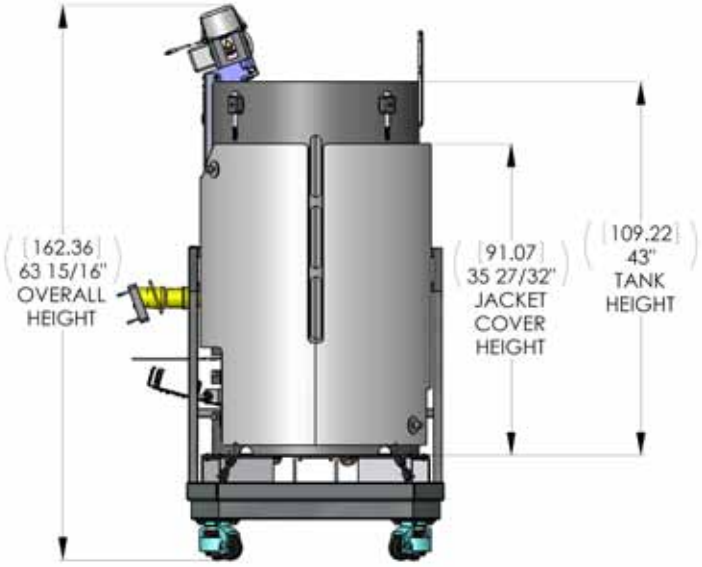
250 L S.U.B. Electric Resistive Heater:





250 L S.U.B. Water Jacket:





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Thermo SCIENTIFIC

3.3.2 250 L Hardware Specifications Electric Resistive Heater

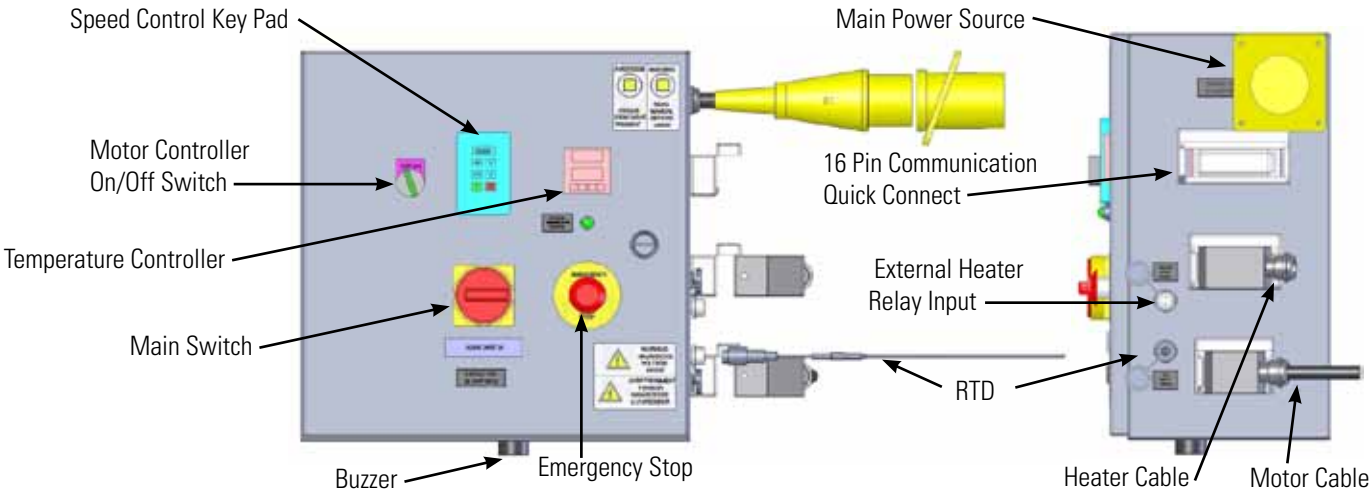
Reactor Geometry	Rated Liquid Working Volume	(250 liter)
	Minimum Liquid Working Volume	(125 liter)
	Total Reactor Volume	(316 liter)
	BPC Chamber Diameter	23.5" (59.7 cm)
	BPC Chamber Shoulder Height	45.5" (115.6 cm)
	Liquid Height @ Rated Working Volume	36" (91.4 cm)
	Fluid Geometry @ Working Volume (height/diameter) Ratio	1.5
	Overall Reactor Geometry (height/diameter) Ratio	1.9
	Tank Baffles	no
Impeller	Impeller (quantity X blade count)	1 X 3
	Impeller Scaling (impeller diameter/tank diameter)	1/3
	Impeller Blade Pitch (angle)	45°
	Impeller Diameter	7.875" (20.0 cm)
	Impeller - Calculated Power Number (N)	2.1
Agitation Parameters	Maximum Mixing Rate (revolutions per minute)	30-200 rpm
	Nominal Agitation Rating - Power/Volume Ratio	0.1 hp/1000 gal (19.7 W/1000 liter)
	Nominal Agitation (revolutions per minute)	118 rpm
	Nominal Tip Speed	243.3 ft/min (123.6 cm/s)
	Counterclockwise Mixing Flow Direction	down-pumping
	Agitation Shaft Resolved Angle	19.6°
	Agitation Shaft Centerline Offset	1.30" (3.3 cm)
	Overall Drive Shaft Length	42" (106.7 cm)
	Operational Drive Shaft Length	36" (91.4 cm)
	Drive Shaft Diameter	0.5" (1.27cm)
	Drive Shaft Poly-Sheath Outside Diameter	1" (2.54 cm)
	Impeller Clearance from Tank Bottom	7.875" (20.0 cm)
Motor	Agitation Motor Drive (type, voltage, phase)	Induction, 208 VAC, three
	Motor Power Rating	0.25 hp (186.4 kW)
	Motor Torque Rating	102 in-lbs (11.5 Nm)
	Gear Reduction	12.5:1
	Programmable VFD, Remote Panel Interface, Power Fault Auto-Restart	standard
	Motor Communication Methods (for external controller)	0-10V, 4-20 mA, ModBus
Temp Control	Programmable PID Temperature Controller	standard
	RTD or Thermocouple, 1/8" (3.18 mm) OD	RTD: Pt-100 (standard)
	Heater Style	resistive
	Solid State Relay (discrete voltage signal)	24-240V AC/DC
	Heater Power Rating	1300 W
	Approximate Liquid Heat-Up Time: (2-37°C)	8 hr
Support Container	Overall Width	26" (66.0 cm)
	Overall Length	35" (88.9 cm)
	Overall Height	60" (152.4 cm)
	Dry Skid Weight (mass)	440 lbs (200 kg)
	Wet Skid Weight—Rated Working Volume (mass)	991 lbs (450 kg)
General	Electrical Power Supply Requirement (voltage, phase, amp)	120/240 VAC, single, 20/10 A
	Operating Temperature (with heater)	Ambient to 40 +/- 0.1 °C (104 +/- 0.2 °F)
	Validated System Reliability (minimum)	0.9 @ 90%

3.3.3 250 L Hardware Specifications Water Jacket

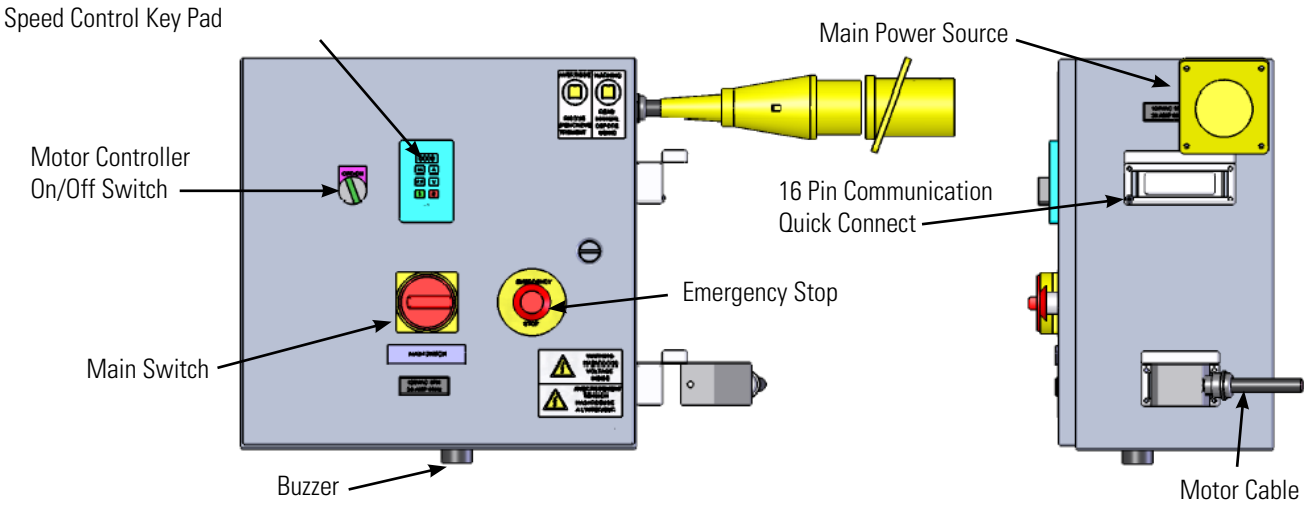
Reactor Geometry	Rated Liquid Working Volume	(250 liter)
	Minimum Liquid Working Volume	(125 liter)
	Total Reactor Volume	(316 liter)
	BPC Chamber Diameter	23.5" (59.7 cm)
	BPC Chamber Shoulder Height	45.5" (115.6 cm)
	Liquid Height @ Rated Working Volume	36" (91.4 cm)
	Fluid Geometry @ Working Volume (height/diameter) Ratio	1.5
	Overall Reactor Geometry (height/diameter) Ratio	1.9
	Tank Baffles	no
Impeller	Impeller (quantity X blade count)	1 X 3
	Impeller Scaling (impeller diameter/tank diameter)	1/3
	Impeller Blade Pitch (angle)	45°
	Impeller Diameter	7.875" (20.0 cm)
	Impeller - Calculated Power Number (N)	2.1
Agitation Parameters	Maximum Mixing Rate (revolutions per minute)	30-150 rpm
	Nominal Agitation Rating - Power/Volume Ratio	0.1 hp/1000 gal (19.7 W/1000 liter)
	Nominal Agitation (revolutions per minute)	118 rpm
	Nominal Tip Speed	243.3 ft/min (123.6 cm/s)
	Counterclockwise Mixing Flow Direction	down-pumping
	Agitation Shaft Resolved Angle	19.6°
	Agitation Shaft Centerline Offset	1.30" (3.3 cm)
	Overall Drive Shaft Length	42" (106.7 cm)
	Operational Drive Shaft Length	36" (91.4 cm)
	Drive Shaft Diameter	0.5" (1.27cm)
	Drive Shaft Poly-Sheath Outside Diameter	1" (2.54 cm)
	Impeller Clearance from Tank Bottom	7.875" (20.0 cm)
Motor	Agitation Motor Drive (type, voltage, phase)	Induction, 208 VAC, three
	Motor Power Rating	0.25 hp (186.4 kW)
	Motor Torque Rating	102 in-lbs (11.5 Nm)
	Gear Reduction	12.5:1
	Programmable VFD, Remote Panel Interface, Power Fault Auto-Restart	standard
	Motor Communication Methods (for external controller)	0-10V, 4-20 mA, ModBus
Temp Control	Jacket type	Low profile Stainless Steel Laser Dimpled Jacket with ExteriorInsulation Shield
	Jacket area: full/half volume (ft^2)	13.6/5.8
	Jacket Volume (L)	1.0 liters
	Jacket Flow Rate at 50 psi	10.25 liters/min
	RTD or Thermocouple, 1/8" (3.18 mm) OD	RTD: Pt-100 (standard)
	Process Connection	3/4" MNPT nipple with Hansen quick connect check valves
	Nominal heating/cooling load (W)	2500
	Nominal heating/cooling time [5-37C] (hr)	5.1
Support Container	Overall Width	26" (66.0 cm)
	Overall Length	35" (88.9 cm)
	Overall Height	60" (152.4 cm)
	Dry Skid Weight (mass)	440 lbs (200 kg)
	Wet Skid Weight—Rated Working Volume (mass)	991 lbs (450 kg)
General	Electrical Power Supply Requirement (voltage, phase, amp)	120/240 VAC, single, 10 A
	Operating Temperature (with heater)	Ambient to 40 +/- 0.1 °C (104 +/- 0.2 °F)
	Validated System Reliability (minimum)	0.9 @ 90%

3.3.4 250 L Control Panel Layout

250 L Control Panel Electric Resistive Heater



250 L Control Panel Water Jacket



3.4 500 L Single-Use Bioreactor

Data Sheet 030 Rev 3

Thermo Scientific HyClone Single-Use Bioreactor (S.U.B.) 500 L

The Thermo Scientific HyClone Single-Use Bioreactor (S.U.B.) is the leading single-use alternative to conventional stirred tank bioreactors for animal and insect cell culture. The current range includes units with maximum working volumes of 50, 100, 250, 500, 1000 and 2000 L. The S.U.B. is now available with new optimized standard BioProcess Containers with improved dual sparge capability. Open pipe and frit sparging systems are now included to provide a wider range of operating conditions.

Overview:

The HyClone® S.U.B. provides all the advantages of single-use bioprocessing without having to buy a complete new bioreactor system. The critical design parameters of the S.U.B., such as height to diameter ratios, mixer design and location and typical control system interfaces, have been maintained.

The S.U.B. BioProcess Container™ (BPC®) is supplied sterilized by irradiation and therefore does not require any facility hook-ups for sterilization or cleaning. A key element to the single-use design is the plastic (polyethylene) impeller with a bearing/seal assembly linked to an external mixer drive.

500 L Water Jacket S.U.B.

This document covers S.U.B. systems with a maximum working volume of 500 L and the new optimized standard S.U.B.s with dual sparge capability which provide a wider range of k_La values, better pH control and lower foaming than the original disk sparger.

The S.U.B. system consists of the following components:

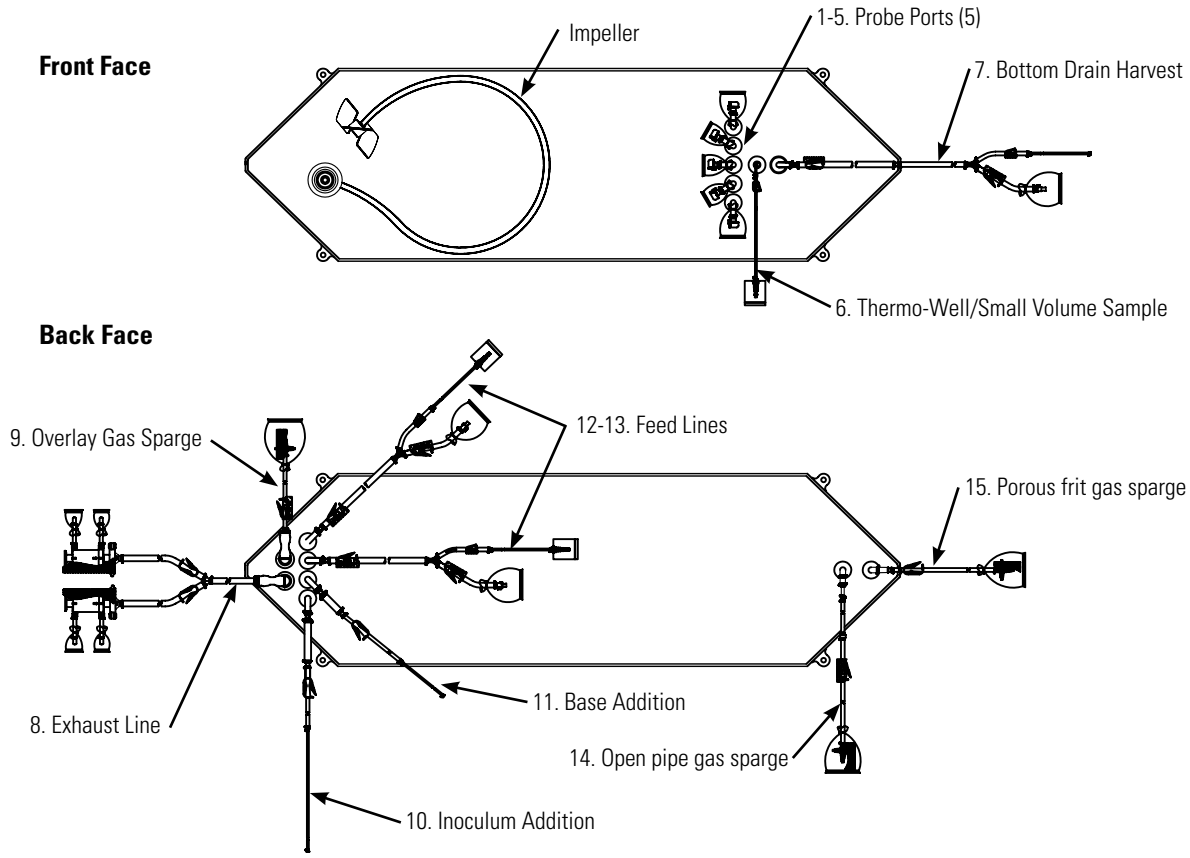
1. Outer Support Container—with a mixer drive complete with control unit and an electrical heater or water jacket.
2. Single-Use Bioreactor BPC—complete with agitator assembly, sparger, vent filter inlet and outlet ports, plus ports for integration of sensor probes and line sets. The S.U.B. BPC is supplied sterile and ready-to-use.
3. Drive Shaft—inserted into the S.U.B. BPC through the mixing drive motor and locked into the disposable agitator assembly.
4. Process Controls—temperature (not on water jacket) and agitation control are integrated into the S.U.B., but additional pH or dissolved oxygen (DO) controls must be supplied by the user.

Item	500 L Electric Resistive Heater	500 L Water Jacket
Rated Liquid Working Volume	500 L	
Minimum Liquid Working Volume	250 L	
Total Reactor Volume (Liquid & Gas)	660 L	
BPC Chamber Diameter	29.75" (75.56 cm)	
BPC Chamber Shoulder Height	57" (144.78 cm)	
Liquid Height @ Rated Working Volume	44.63" (113.36 cm)	
Overall Reactor Geometry (height/diameter ratio)	1.9:1	
Fluid Geometry @ Working Volume (height/diameter ratio)	1.5:1	
Impeller (quantity x blade count)	1 x 3	
Impeller Diameter	9.88" (25.09 cm)	
pH & DO Probe— Autoclavable Type (Applisens, Broadley James, Metler Toledo)	12 mm diameter x 215-235 mm insertion length x 13.5 PG thread	
Hold-Up Volume	< 1 L	
Electrical Power Supply Requirement (voltage, phase, amp)	208/240 VAC, single, 20 A	208/240 VAC, single, 10 A
Overall Width	39.22" (99.61 cm)	
Overall Length	52.12" (132.38 cm)	
Overall Height	91" (231.14 cm)	
S.U.B. Recommended Operating Parameters		
Operating Temperature Range	Ambient to 40 +/- 0.1°C (104 +/- 0.2°F)	
Motor Speed	30-150 rpm	
Volume Range	250-500 L	
Maximum Bag Pressure	0.5 psi (0.03 bar)	
Continuous Operating Time	21 days*	

*Mixing time at nominal volume only.

Standard BPC Configurations (SH30774.04)

For use with tubing welder, CPC Quick Connect



Standard BPC Configurations

For use with tubing welder and CPC Quick Connects

Line	Description	Tubing Set (ID X OD X Length)	End Treatment
1-5	Probe Ports (5)	1/2" (12.7 mm) Tube ports	Pall® Kleenpak™ aseptic connectors—KPCHT Series (Female)
6	Thermo-Well/ Small Volume Sample	Thermo-Well Adapter for 1/4" (6.4 mm) Diameter. 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex® X 24" (60 cm)	SterilEnz® Pouch with injection site assembly
7	Bottom Drain Harvest	1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 60" (152 cm) reduced to 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 12" (30 cm) splits to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 12" 30 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm) and 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 12" (30 cm)	Plugged 3/8" MPC Insert
8	Exhaust Line	1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 4" (10 cm) splits to 1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 10" (25 cm) and 1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 10" (25 cm)	(2) Pall Kleenpak 0.2 Micron Exhaust Vent Filter
9	Overlay Gas Sparge	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 6" (15 cm)	Hydrophobic vent filter with Emflon® II
10	Inoculum Addition	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 84" (213 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm)	Plugged
11	Base Addition	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 6" (15 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 84" (213 cm)	Plugged
12-13	Feed Lines	3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 84" (213 cm) splits to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 12" (30 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm) and 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 12" (30 cm)	SterilEnz Pouch with injection site assembly 3/8" MPC Body
14	Open Pipe Gas Sparge	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 3" (8 cm) reduced to Check Valve and 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 72" (183 cm)	Hydrophobic vent filter with Emflon II
15	Porous frit gas sparge 12 mm dia (25 µm pores)	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 6" (15 cm) reduced to Check Valve and 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 72" (183 cm)	Hydrophobic vent filter with Emflon II

Ordering Information for Standard BPC Products

Custom BPC Options:

Category	Options/Capability	Remarks
Tubing Type	C Flex, platinum cured silicone, PVC, Pharmed®, PharmaPure®	More information in selection guide of BPC catalog
Tubing Size	Specific lengths of 1/8" ID to 1" ID	ID limitations due to port size
Connectors	Luers, CPC Quick Connects, SIP connectors, Triclamp, Kleenpak, Lynx®, SmartSite®, Clave®, Lynx steam thru, CPC Steam Thru, Gore steam valve, Gore Mini TC, BioQuate (GE), PAW SterilEnz®, end plug, etc.	Refer to selection guide in BPC catalog for further information by connection type. **Note:** Only option for probe port connections is Kleenpak.
Kleenpak (i.e., probe) ports	Additional ports: second row of 4 for 50 L to 250 L S.U.Bs.; second row of 5 for 500 L and 1000 L S.U.B.s	
Disposable sensors	Pressure sensor: Pendotech for 50 L to 250 L S.U.B. (comes standard on 500 L and 1000 L) DO – Finesse DO and pH – PreSens Availability of various other disposable sensors currently pending.	
Addition of ports/lines (other than 2nd row of probe ports)	Limited engineer-to-order customization possible such as additional media lines and vent filter lines. Requires economic justification.	Dependent on location in bag and compatibility with hardware
Port sizes	Limited customization possible as engineer-to-order with justification.	Dependent on location in bag and fit with hardware (e.g., 1" ID port on harvest line)
Re-arrangement of lines on existing ports	Limited customization possible, e.g., moving sample/tempwell port to a probe tube port, or swapping overlay inlet line with supplement line.	Dependent on location in bag and fit with hardware
Sparger	Dual sparger (open pipe plus porous frit) standard. Can do an engineer-to-order for one or the other alone. Make-to-order bags will be built around standard dual sparger chamber.	
Dip tube lines	Limited customization possible. Suggested use through 1" port, so this is engineer-to-order. Otherwise must use ferrule approach.	Length cannot interfere with impeller and shaft. Typical is 10" or shorter.
Overlay and Sparge Line Filters	Can use disposable (capsule) filter other than standard hydrophobic vent filter with Emflon II.	
Vent Filters	Standard is Pall Kleenpak 0.2 micron exhaust vent filter.	**Note:** Vent filter heater configuration restricts options
Vent Filter Tubing Length	Extended filter height above the S.U.B. bag is make-to-order.	Must be compatible with a vent filter bracket option
Filters on Media and Supplement Inlets	Choice of filters for inlets used to sterile filter incoming media or supplements.	

Please Note: Not all options are available for all ports. No customization of port type and location, chamber dimensions or mixing assembly is possible. For additional information, please see the Selection Guides in the S.U.B. BPC Catalog.

Presentation (as dry BPC systems):

Outer Packaging	Supplied 'flat-packed' Two polyethylene outer layers
Label	Description Product code Lot number Expiry date on outer packaging and shipping container
Sterilization	Irradiation (25 to 38 kGy) inside outer packaging
Shipping Container	Durable cardboard carton
Documentation	Certificate of Analysis provided with each lot for each delivery

Hardware Standard Products

Electric Resistive Heater:

Part Number	Description	
SV50200.02	500 L S.U.B., (240 VAC, Single Phase)	Includes: 304 stainless steel outer support container with swivel caster platform, variable speed agitation controller, motor, drive assembly with shaft, PID temperature controller, RTD sensor, integrated resistive heating element, probe shelf and standard tool set

Water Jacket:

Part Number	Description	
SV50200.04	500 L S.U.B., (240 VAC, Single Phase)	Includes: 304 stainless steel outer support container with swivel caster platform, variable speed agitation controller, motor, drive assembly with shaft, RTD sensor, integrated water jacket, probe shelf and standard tool set

Custom Options

Custom Hardware Options:

For stainless steel capabilities, please contact your sales representative for HyClone products for more information.

Accessories

Part Number	Description	
SH30720.01	Bioreactor Probe Assembly (non-sterile)	Used to package the pH and DO probes (not supplied) for sterilization and to aseptically connect them to the S.U.B. BPC. See Figure 1.
SV20664.01	Heavy Duty Tubing Clamp	Reusable tubing clamp used on probe ports when connecting probe assemblies.
SV20664.02	Heavy Duty Tubing Clamp (4 pack of SV20664.01)	
SV20664.03	Heavy Duty Tubing Clamp (10 pack of SV20664.01)	
SV20750.01	S.U.B. Temperature/Sample Port	Used for RTD calibration/validation.
SV50177.01	Autoclave Tray for Probe Kits (stainless steel)	Support tray which allows the probes to be safely autoclaved. See Figure 2.
SH30845.01	Sterile Sampling Manifold with luer lock (individual)	Available for aseptic luer connection or weld onto the sample line to take sample sets.
SH30845.02	Sterile Sampling Manifold with luer lock (10 pack)	
SV50177.65	Frit Sparge Line Support	Recommended to maintain the frit sparge in a vertical position.
SV50177.17	Elevated Dual Filter Bracket	Needed to support elevated dual vent filters.

Figure 1
Bioreactor Probe Assembly

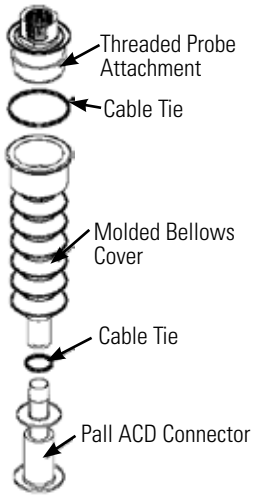
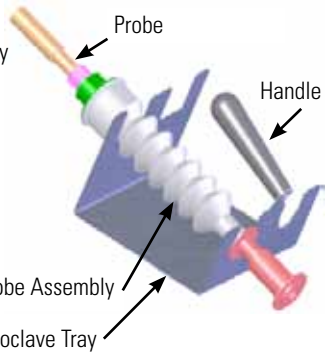


Figure 2
Autoclave Tray for Probe Kits



Additional information on autoclave tray:

- Fabricated from stainless steel
- Plastic carry handle for easy transport right out of the autoclave
- Positions probes on 15% incline for greater probe/membrane longevity
- Will restrain probe bellows from collapsing during sterilization
- Probe holder accommodates two probes

Figure 3
Elevated Dual Filter Bracket

Figure 4
Frit Sparge Line Support

Single-Use Bioreactor (S.U.B.) First Time Operator—Recommended Parts List

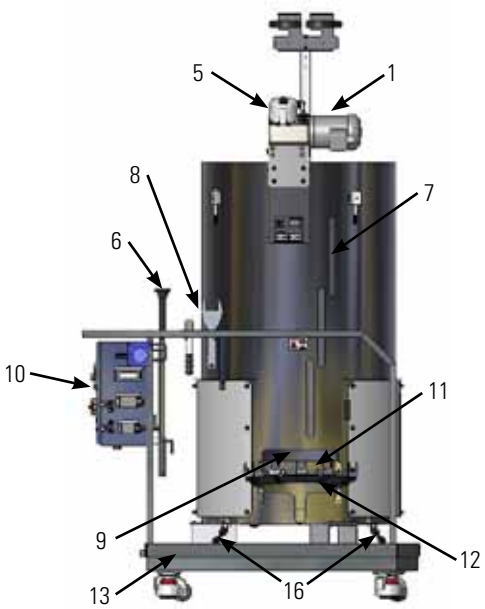
Available Parts (consumables sufficient for three complete cell culture runs)		
Part Number	**Description**	**Quantity**
SV50200 (500 L)	S.U.B. Hardware System (standard)	1
SH30774.04	S.U.B. BPC (standard)	3
SH30720.01	Bioreactor Probe Assembly (non-sterile for use in autoclave)	12
SV20664.03	Heavy Duty Tubing Clamp (10 pack)	1
SV50177.01	Autoclave Tray for Autoclaving Probe Kits	2
SV20750.01	S.U.B. Temperature Port (used to verify RTD calibration)	1
SH30845.02	Sterile Sampling Manifold with Luer Locks (10 pack)	3
Auxiliary Components Supporting The Single-Use Bioreactor		
Description	**Purpose**	**Quantity**
Bioreactor control system	Necessary for regulation of gas pressure and flow rate control for DO and pH set points	1
DO probe	Autoclavable Probe (13 mm X 13.5PG thread w/ 195-235 mm insertion length)	1
pH probe	Autoclavable Probe (13 mm X 13.5PG thread w/ 195-235 mm insertion length)	1
Sterile/Aseptic Connection Method	Tubing Welder (Terumo or Wave), Steam In Place (SIP) Sterilizer, or Laminar Flow Hood	1
Peristaltic Pump	Used for fluid transfer between line sets and containers	1
Temperature Control Unit (TCU)	Necessary for water jacket temperature control (not provided)	1

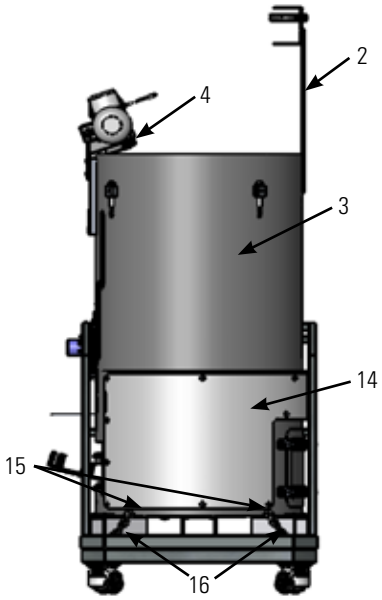
Hardware Features

500 L with Electric Resistive Heater:

The stainless steel outer support container contains the following features:

1. Mixer motor
2. Exhaust vent filter holder
3. Stainless steel (304) outer support container
4. Bearing port receiver with clamp
5. Mixing assembly with shield
6. Drive shaft
7. Liquid sight window
8. Standard tool set
9. Probe access window
10. Control panel
11. Probe holder
12. Probe shelf
13. Platform with swivel casters and leveling pads
14. Resistive heater w/heat shield
15. Bottom cut outs for BPC alignment
16. Stretch hooks



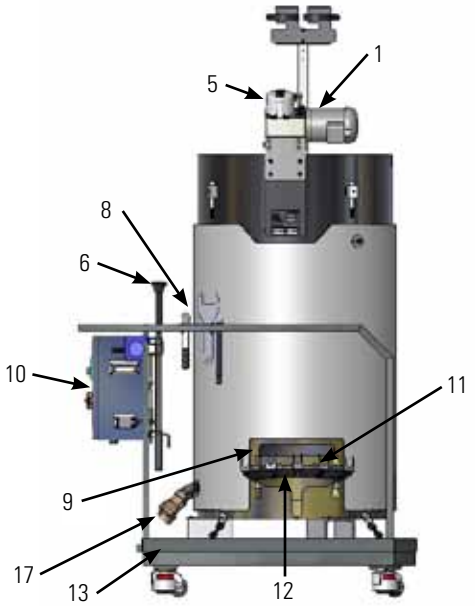


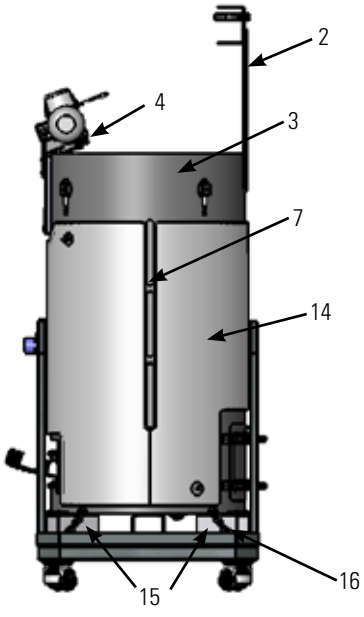
Hardware Features

500 L with Water Jacket:

The stainless steel outer support container contains the following features:

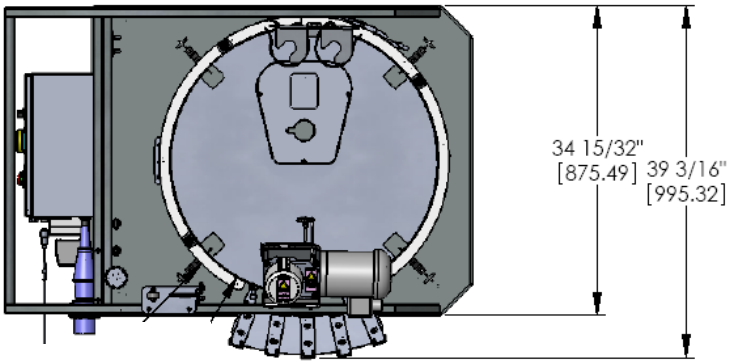
1. Mixer motor
2. Exhaust vent filter holder
3. Stainless steel (304) outer support container
4. Bearing port receiver with clamp
5. Mixing assembly with shield
6. Drive shaft
7. Liquid sight window
8. Standard tool set
9. Probe access window
10. Control panel
11. Probe holder
12. Probe shelf
13. Platform with swivel casters and leveling pads
14. Laser dimple water jacket
15. Bottom cut outs for BPC alignment
16. Stretch hooks
17. Jacket quick connect couplings

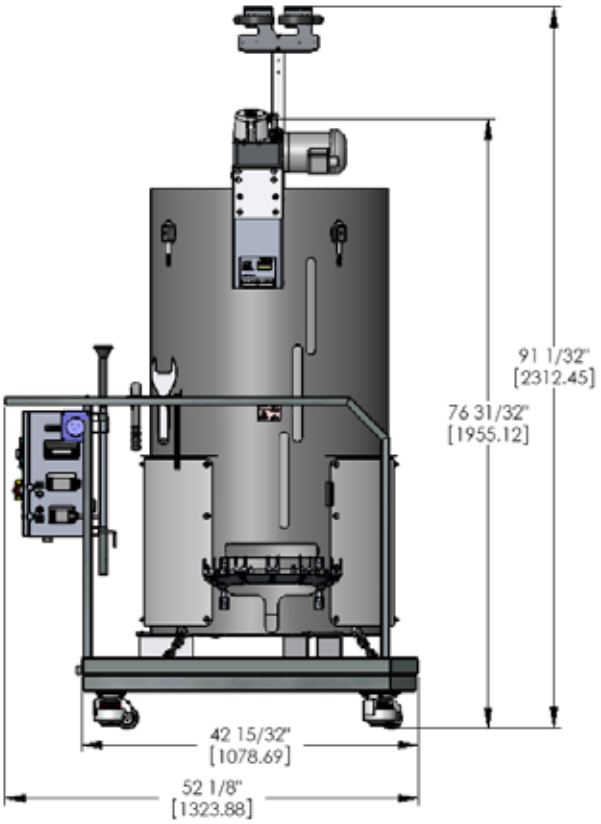




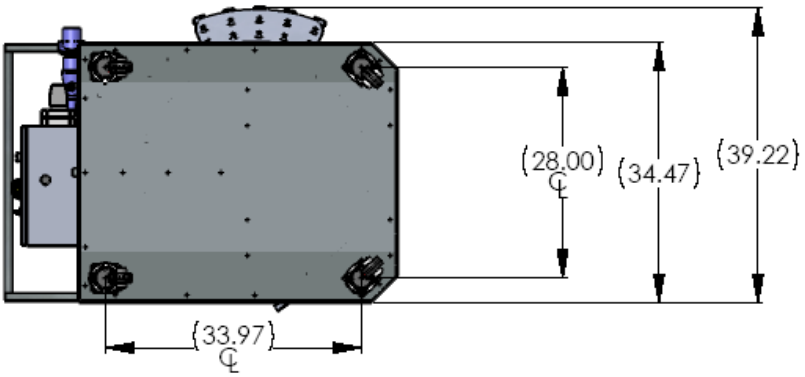
Outer Support Container (units in inches [mm])

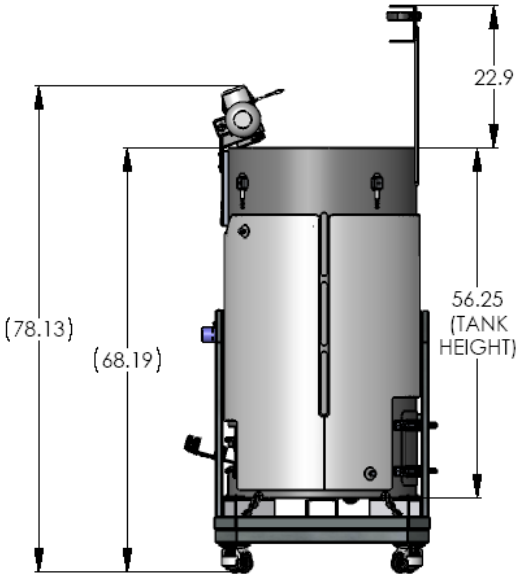
500 L S.U.B. Electric Resistive Heater:





500 L S.U.B. Water Jacket:





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Thermo SCIENTIFIC

3.4.2 500 L Hardware Specifications Electric Resistive Heater

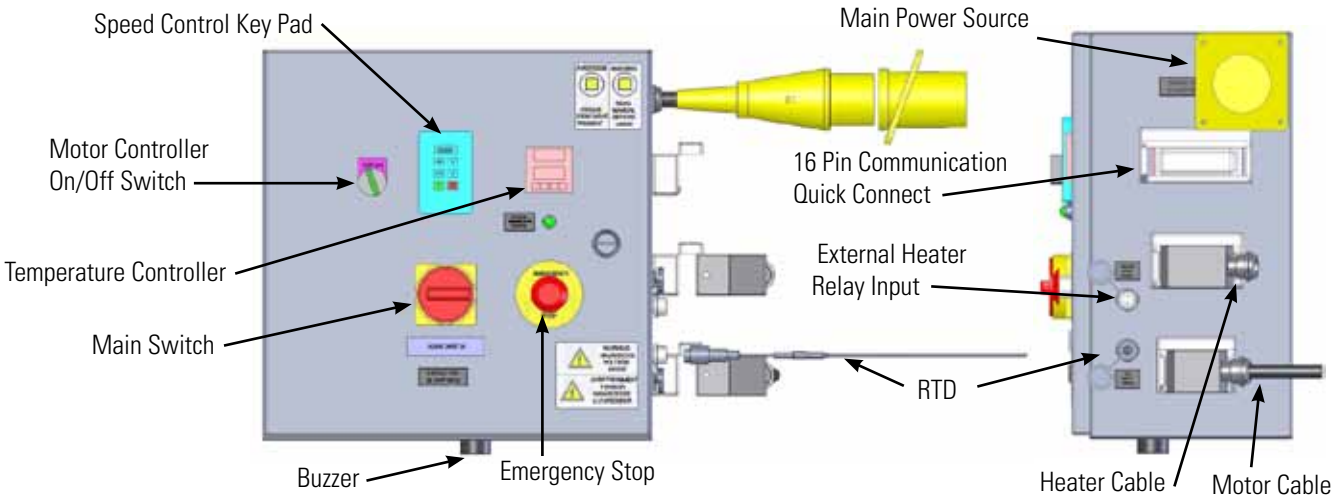
Reactor Geometry	Rated Liquid Working Volume	(500 liter)
	Minimum Liquid Working Volume	(250 liter)
	Total Reactor Volume	(660 liter)
	BPC Chamber Diameter	29.75" (75.6 cm)
	BPC Chamber Shoulder Height	60" (152.4 cm)
	Liquid Height @ Rated Working Volume	44.63" (113.4 cm)
	Fluid Geometry @ Working Volume (height/diameter) Ratio	1.5
	Overall Reactor Geometry (height/diameter) Ratio	1.9
	Tank Baffles	no
Impeller	Impeller (quantity X blade count)	1 X 3
	Impeller Scaling (impeller diameter/tank diameter)	1/3
	Impeller Blade Pitch (angle)	45°
	Impeller Diameter	9.875" (25.1 cm)
	Impeller - Calculated Power Number (N)	2.1
Agitation Parameters	Maximum Mixing Rate (revolutions per minute)	30-150 rpm
	Nominal Agitation Rating - Power/Volume Ratio	0.1 hp/1000 gal (19.7 W/1000 liter)
	Nominal Agitation (revolutions per minute)	100 rpm
	Nominal Tip Speed	270 ft/min (137.2 cm/s)
	Counterclockwise Mixing Flow Direction	down-pumping
	Agitation Shaft Resolved Angle	19.6°
	Agitation Shaft Centerline Offset	2" (5.08 cm)
	Overall Drive Shaft Length	50" (127.0 cm)
	Operational Drive Shaft Length	44" (111.76 cm)
	Drive Shaft Diameter	0.75" (1.90 cm)
	Drive Shaft Poly-Sheath Outside Diameter	1.375" (3.49 cm)
	Impeller Clearance from Tank Bottom	9.875" (25.0 cm)
Motor	Agitation Motor Drive (type, voltage, phase)	Induction, 208 VAC, three
	Motor Power Rating	0.50 hp (372.8 kW)
	Motor Torque Rating	82 in-lbs (9.5 Nm)
	Gear Reduction	10:1
	Programmable VFD, Remote Panel Interface, Power Fault Auto-Restart	standard
	Motor Communication Methods (for external controller)	0-10V, 4-20 mA, ModBus
Temp Control	Programmable PID Temperature Controller	standard
	RTD or Thermocouple, 1/8" (3.18 mm) OD	RTD: Pt-100 (standard)
	Heater Style	resistive
	Solid State Relay (discrete voltage signal)	24-240V AC/DC
	Heater Power Rating	2800 W
	Approximate Liquid Heat-Up Time: (2-37°C)	11 hr
Support Container	Overall Width	39.22" (99.61 cm)
	Overall Length	52.12" (132.38 cm)
	Overall Height	91" (231.14 cm)
	Dry Skid Weight (mass)	591 lbs (268 kg)
	Wet Skid Weight—Rated Working Volume (mass)	1693 lbs (768 kg)
General	Electrical Power Supply Requirement (voltage, phase, amp)	208/240 VAC, single, 20 A
	Operating Temperature (with heater)	Ambient to 40 +/- 0.1 °C (104 +/- 0.2 °F)
	Validated System Reliability (minimum)	0.9 @ 90%

3.4.3 500 L Hardware Specifications Water Jacket

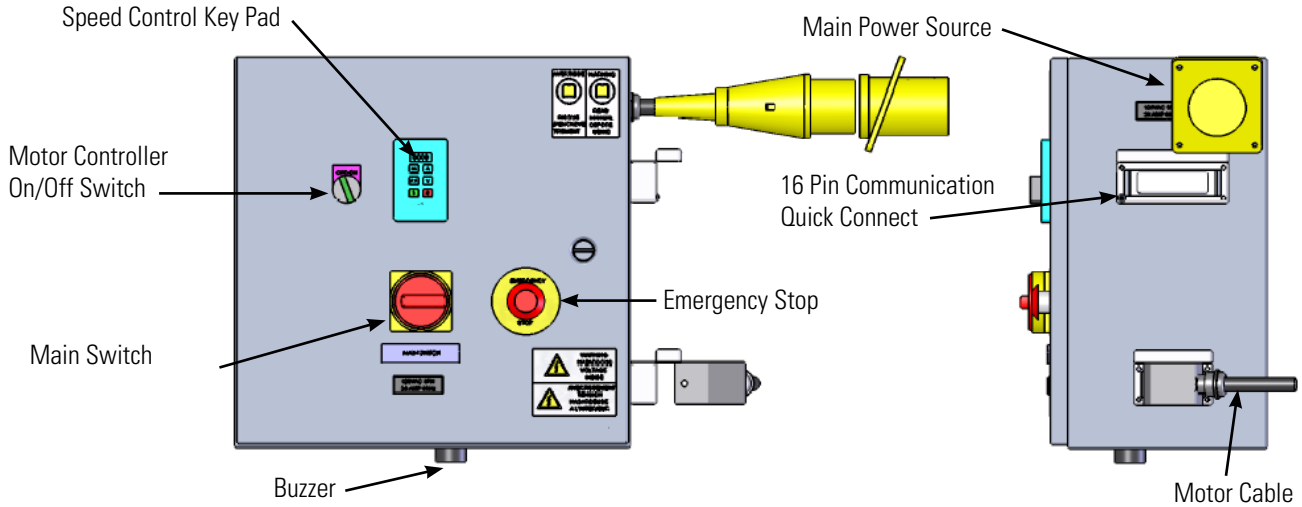
Reactor Geometry	Rated Liquid Working Volume	(500 liter)
	Minimum Liquid Working Volume	(250 liter)
	Total Reactor Volume	(660 liter)
	BPC Chamber Diameter	29.75" (75.6 cm)
	BPC Chamber Shoulder Height	60" (152.4 cm)
	Liquid Height @ Rated Working Volume	44.63" (113.4 cm)
	Fluid Geometry @ Working Volume (height/diameter) Ratio	1.5
	Overall Reactor Geometry (height/diameter) Ratio	1.9
	Tank Baffles	no
Impeller	Impeller (quantity X blade count)	1 X 3
	Impeller Scaling (impeller diameter/tank diameter)	1/3
	Impeller Blade Pitch (angle)	45°
	Impeller Diameter	9.875" (25.1 cm)
	Impeller - Calculated Power Number (N)	2.1
Agitation Parameters	Maximum Mixing Rate (revolutions per minute)	30-150 rpm
	Nominal Agitation Rating - Power/Volume Ratio	0.1 hp/1000 gal (19.7 W/1000 liter)
	Nominal Agitation (revolutions per minute)	100 rpm
	Nominal Tip Speed	270 ft/min (137.2 cm/s)
	Counterclockwise Mixing Flow Direction	down-pumping
	Agitation Shaft Resolved Angle	19.6°
	Agitation Shaft Centerline Offset	2" (5.08 cm)
	Overall Drive Shaft Length	50" (127.0 cm)
	Operational Drive Shaft Length	44" (111.76 cm)
	Drive Shaft Diameter	0.75" (1.90 cm)
	Drive Shaft Poly-Sheath Outside Diameter	1.375" (3.49 cm)
	Impeller Clearance from Tank Bottom	9.875" (25.0 cm)
Motor	Agitation Motor Drive (type, voltage, phase)	Induction, 208 VAC, three
	Motor Power Rating	0.50 hp (372.8 kW)
	Motor Torque Rating	82 in-lbs (11.5 Nm)
	Gear Reduction	5:1
	Programmable VFD, Remote Panel Interface, Power Fault Auto-Restart	standard
	Motor Communication Methods (for external controller)	0-10V, 4-20 mA, ModBus
Temp Control	Jacket type	Low profile Stainless Steel Laser Dimpled Jacket with Exterior Insulation Shield
	Jacket area: full/half volume (ft^2)	21.4/8.4
	Jacket Volume (L)	1.75 liters
	Jacket Flow Rate at 50 psi	40 liters/min
	RTD or Thermocouple, 1/8" (3.18 mm) OD	RTD: Pt-100 (standard)
	Process Connection	3/4" MNPT nipple with Hansen quick connect check valves
	Nominal heating/cooling load (W)	5000
	Nominal heating/cooling time [5-37C] (hr)	3.5
Support Container	Overall Width	39.22" (99.61 cm)
	Overall Length	52.12" (132.38 cm)
	Overall Height	91" (231.14 cm)
	Dry Skid Weight (mass)	724 lbs (328 kg)
	Wet Skid Weight—Rated Working Volume (mass)	1826 lbs (828 kg)
General	Electrical Power Supply Requirement (voltage, phase, amp)	208/240 VAC, single, 10 A
	Operating Temperature (with heater)	5 to 40 +/- 0.1 °C (104 +/- 0.2 °F)
	Validated System Reliability (minimum)	0.9 @ 90%

3.4.4 500 L Control Panel Layout

500 L Control Panel Electric Resistive Heater



500 L Control Panel Water Jacket



3.5 1000 L Single-Use Bioreactor

Data Sheet 034 Rev 8

Thermo Scientific HyClone Single-Use Bioreactor (S.U.B.) 1000 L

The Thermo Scientific HyClone Single-Use Bioreactor (S.U.B.) is the leading single-use alternative to conventional stirred tank bioreactors for animal and insect cell culture. The current range includes units with maximum working volumes of 50, 100, 250, 500, 1000 and 2000 L. The S.U.B. is now available with new optimized standard BioProcess Containers with improved dual sparge capability. Open pipe and frit sparging systems are now included to provide a wider range of operating conditions.

Overview:

The HyClone® S.U.B. provides all the advantages of single-use bioprocessing without having to buy a complete new bioreactor system. The critical design parameters of the S.U.B., such as height to diameter ratios, mixer design and location and typical control system interfaces, have been maintained.

The S.U.B. BioProcess Container™ (BPC®) is supplied sterilized by irradiation and therefore does not require any facility hook-ups for sterilization or cleaning. A key element to the single-use design is the plastic (polyethylene) impeller with a bearing/seal assembly linked to an external mixer drive.

1000 L Water Jacket S.U.B.

This document covers S.U.B. systems with a maximum working volume of 1000 L and the new optimized standard S.U.B.s with dual sparge capability which provide a wider range of k_La values, better pH control and lower foaming than the original disk sparger.

The S.U.B. system consists of the following components:

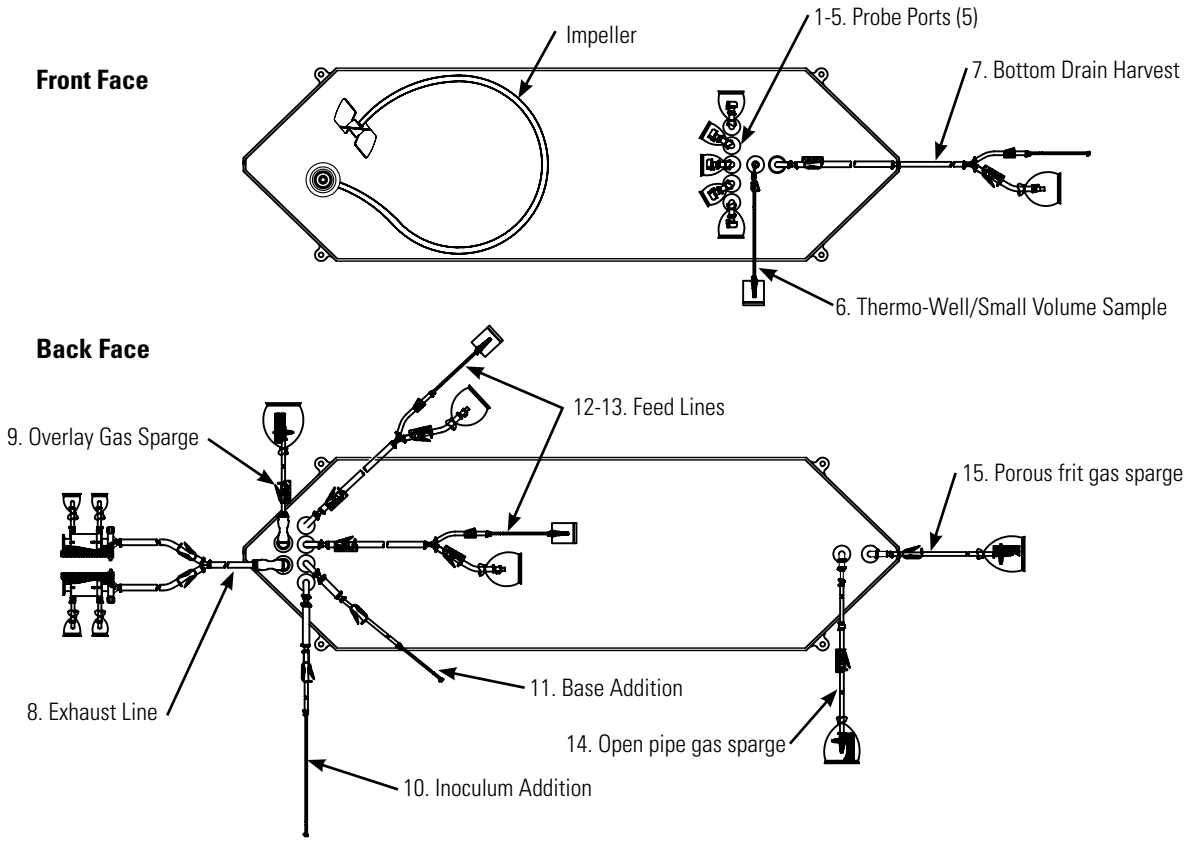
1. Outer Support Container—with a mixer drive complete with control unit and an electrical heater or water jacket.
2. Single-Use Bioreactor BPC—complete with agitator assembly, sparger, vent filter inlet and outlet ports, plus ports for integration of sensor probes and line sets. The S.U.B. BPC is supplied sterile and ready-to-use.
3. Drive Shaft—inserted into the S.U.B. BPC through the mixing drive motor and locked into the disposable agitator assembly.
4. Process Controls—temperature (not on water jacket) and agitation control are integrated into the S.U.B., but additional pH or dissolved oxygen (DO) controls must be supplied by the user.

Item	1000 L Electric Resistive Heater	1000 L Water Jacket
Rated Liquid Working Volume	1000 L	
Minimum Liquid Working Volume	500 L	
Total Reactor Volume (Liquid & Gas)	1320 L	
BPC Chamber Diameter	37.75" (95.9 cm)	
BPC Chamber Shoulder Height	79" (200.7 cm)	
Liquid Height @ Rated Working Volume	56" (142.2 cm)	
Overall Reactor Geometry (height/diameter ratio)	1.9:1	
Fluid Geometry @ Working Volume (height/diameter ratio)	1.5:1	
Impeller (quantity x blade count)	1 x 3	
Impeller Diameter	12.625" (32.1 cm)	
pH & DO Probe— Autoclavable Type (Applisens, Broadley James, Metler Toledo)	12 mm diameter x 215-235 mm insertion length x 13.5 PG thread	
Hold-Up Volume	< 4 L	
Electrical Power Supply Requirement (voltage, phase, amp)	208-240 VAC, single, 30 A	208-240 VAC, single, 30 A
Overall Width	40" (101.6 cm)	46" (116.8 cm)
Overall Length	51" (131.9 cm)	60" (153.4 cm)
Overall Height	90" (228.6 cm)	90" (228.6 cm)
S.U.B. Recommended Operating Parameters		
Operating Temperature Range	Ambient to 40 +/- 0.1°C (104 +/- 0.2°F)	
Motor Speed	20-110 rpm	
Volume Range	500-1000 L	
Maximum Bag Pressure	0.5 psi (0.03 bar)	
Continuous Operating Time	21 days*	

*Mixing time at nominal volume only.

Standard BPC Configuration (SH30774.05)

For use with tubing welder and CPC Quick Connects (see page 3 for line details)



Standard BPC Configuration (CX5-14 Film)

For use with tubing welder and CPC Quick Connects

Line	Description	Tubing Set (ID X OD X Length)	End Treatment
1-5	Probe Ports (5)	1/2" (12.7 mm) Tube ports	Pall® Kleenpak™ aseptic connectors—KPCHT Series (Female)
6	Thermo-Well/ Small Volume Sample	Thermo-Well Adapter for 1/4" (6.4 mm) Diameter. 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex® X 24" (60 cm)	SterilEnz® Pouch with injection site assembly
7	Bottom Drain Harvest	1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 60" (152 cm) reduced to 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 12" (30 cm) splits to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 12" 30 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm) and 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 12" (30 cm)	Plugged 3/8" MPC Insert
8	Exhaust Line	1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 4" (10 cm) splits to 1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 10" (25 cm) and 1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 10" (25 cm)	(2) Pall Kleenpak 0.2 Micron Exhaust Vent Filter
9	Overlay Gas Sparge	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 6" (15 cm)	Hydrophobic vent filter with Emflon® II, Pressure Transducer
10	Inoculum Addition	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 84" (213 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm)	Plugged
11	Base Addition	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 6" (15 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 84" (213 cm)	Plugged
12-13	Feed Lines	3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 84" (213 cm) splits to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 12" (30 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm) and 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 12" (30 cm)	Sterilenz Pouch with injection site assembly 3/8" MPC Body
14	Open Pipe Gas Sparge	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 3" (8 cm) reduced to Check Valve and 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 72" (183 cm)	Hydrophobic vent filter with Emflon II
15	Porous frit gas sparge 12 mm dia (25 µm pores)	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 6" (15 cm) reduced to Check Valve and 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 72" (183 cm)	Hydrophobic vent filter with Emflon II

Ordering Information for Standard BPC Products

Custom BPC Options:

Category	Options/Capability	Remarks
Tubing Type	C Flex, platinum cured silicone, PVC, Pharmed®, PharmaPure®	More information in selection guide of BPC catalog
Tubing Size	Specific lengths of 1/8" ID to 1" ID	ID limitations due to port size
Connectors	Luers, CPC Quick Connects, SIP connectors, Triclamp, Kleenpak, Lynx®, SmartSite®, Clave®, Lynx steam thru, CPC Steam Thru, Gore steam valve, Gore Mini TC, BioQuate (GE), PAW SterilEnz®, end plug, etc.	Refer to selection guide in BPC catalog for further information by connection type. **Note:** Only option for probe port connections is Kleenpak.
Kleenpak (i.e., probe) ports	Additional ports: second row of 4 for 50 L to 250 L S.U.Bs.; second row of 5 for 500 L and 1000 L S.U.B.s	
Disposable sensors	Pressure sensor: Pendotech for 50 L to 250 L S.U.B. (comes standard on 500 L and 1000 L) DO – Finesse DO and pH – PreSens Availability of various other disposable sensors currently pending.	
Addition of ports/lines (other than 2nd row of probe ports)	Limited engineer-to-order customization possible such as additional media lines and vent filter lines. Requires economic justification.	Dependent on location in bag and compatibility with hardware
Port sizes	Limited customization possible as engineer-to-order with justification.	Dependent on location in bag and fit with hardware (e.g., 1" ID port on harvest line)
Re-arrangement of lines on existing ports	Limited customization possible, e.g., moving sample/tempwell port to a probe tube port, or swapping overlay inlet line with supplement line.	Dependent on location in bag and fit with hardware
Sparger	Dual sparger (open pipe plus porous frit) standard. Can do an engineer-to-order for one or the other alone. Make-to-order bags will be built around standard dual sparger chamber.	
Dip tube lines	Limited customization possible. Suggested use through 1" port, so this is engineer-to-order. Otherwise must use ferrule approach.	Length cannot interfere with impeller and shaft. Typical is 10" or shorter.
Overlay and Sparge Line Filters	Can use disposable (capsule) filter other than standard hydrophobic vent filter with Emflon II.	
Vent Filters	Standard is Pall Kleenpak 0.2 micron exhaust vent filter.	**Note:** Vent filter heater configuration restricts options
Vent Filter Tubing Length	Extended filter height above the S.U.B. bag is make-to-order.	Must be compatible with a vent filter bracket option
Filters on Media and Supplement Inlets	Choice of filters for inlets used to sterile filter incoming media or supplements.	

Please Note: Not all options are available for all ports. No customization of port type and location, chamber dimensions or mixing assembly is possible. For additional information, please see the Selection Guides in the S.U.B. BPC Catalog.

Presentation (as dry BPC systems):

Outer Packaging	Supplied 'flat-packed' Two polyethylene outer layers
Label	Description Product code Lot number Expiry date on outer packaging and shipping container
Sterilization	Irradiation (25 to 38 kGy) inside outer packaging
Shipping Container	Durable cardboard carton
Documentation	Certificate of Analysis provided with each lot for each delivery

Hardware Standard Products

Electric Resistive Heater:

Part Number	Description	
SV50174.01	1000 L S.U.B., Modbus Plus Load Cell Interface (240 VAC)	Includes: 304 stainless steel outer support container with swivel caster platform, variable speed agitation controller, motor, drive assembly with 3 piece split drive shaft, PID temperature controller, RTD sensor, integrated resistive heating element, three load cells with summing block/display, BPC pressure monitor, probe shelf, and standard tool set
SV50174.02	1000 L S.U.B., Allen-Bradley Load Cell Interface (240 VAC)	
SV50174.03	1000 L S.U.B., Analog Output Load Cell Interface (240 VAC)	
SV50174.04	1000 L S.U.B., Profibus Load Cell Interface (240 VAC)	
SV50174.05	1000 L S.U.B., DeviceNet Load Cell Interface (240 VAC)	

Water Jacket:

Part Number	Description	
SV50174.11	1000 L S.U.B., Modbus Plus Load Cell Interface (240 VAC)	Includes: 304 stainless steel outer support container with swivel caster platform, variable speed agitation controller, motor, drive assembly with 3 piece split drive shaft, RTD sensor, integrated water jacket, three load cells with summing block/display, BPC pressure monitor, probe shelf, and standard tool set
SV50174.12	1000 L S.U.B., Allen-Bradley Load Cell Interface (240 VAC)	
SV50174.13	1000 L S.U.B., Analog Output Load Cell Interface (240 VAC)	
SV50174.14	1000 L S.U.B., Profibus Load Cell Interface (240 VAC)	
SV50174.15	1000 L S.U.B., DeviceNet Load Cell Interface (240 VAC)	

Custom Options

Custom Hardware Options

For stainless steel capabilities, please contact your sales representative for HyClone products for more information.

Accessories

Part Number	Description	
SH30720.01	Bioreactor Probe Assembly (non-sterile)	Used to package the pH and DO probes (not supplied) for sterilization and to aseptically connect them to the S.U.B. BPC. See Figure 1.
SV20664.01	Heavy Duty Tubing Clamp	Reusable tubing clamp used on probe ports when connecting probe assemblies.
SV20664.02	Heavy Duty Tubing Clamp (4 pack of SV20664.01)	
SV20664.03	Heavy Duty Tubing Clamp (10 pack of SV20664.01)	
SV20750.01	S.U.B. Temperature/Sample Port	Used for RTD calibration/validation.
SV50177.01	Autoclave Tray for Probe Kits (stainless steel)	Support tray which allows the probes to be safely autoclaved. See Figure 2.
SH30845.01	Sterile Sampling Manifold with luer lock (individual)	Available for aseptic luer connection or weld onto the sample line to take sample sets.
SH30845.02	Sterile Sampling Manifold with luer lock (10 pack)	
SV50177.65	Frit Sparge Line Support	Recommended to maintain the frit sparge in a vertical position.
SV50177.17	Elevated Dual Filter Bracket (resistive blanket S.U.B.)	Needed to support elevated dual vent filters.
SV50177.21	Adapter required for SV50177.17	
SV50177.20	Elevated Dual Filter Bracket (jacketed S.U.B.) No adapter required	Needed to support elevated dual vent filters.

Figure 1
Bioreactor Probe Assembly

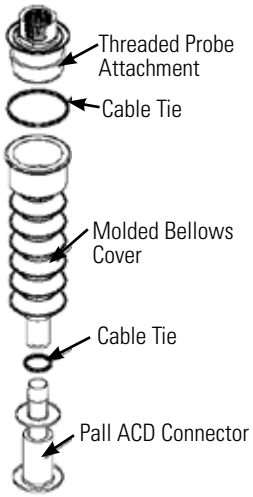
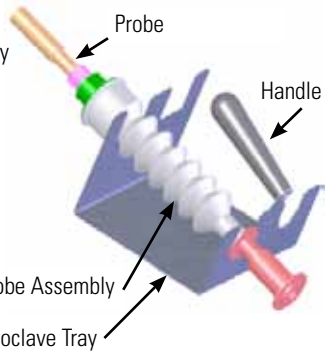


Figure 2
Autoclave Tray for Probe Kits



Additional information on autoclave tray::

- Fabricated from stainless steel
- Plastic carry handle for easy transport right out of the autoclave
- Positions probes on 15% incline for greater probe/membrane longevity
- Will restrain probe bellows from collapsing during sterilization
- Probe holder accommodates two probes

Figure 3
Elevated Dual Filter Bracket (for use with resistive heater S.U.B.)

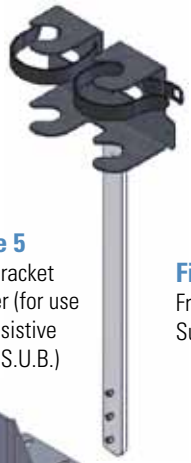


Figure 4
Elevated Dual Filter Bracket (for use with water jacketed S.U.B.)

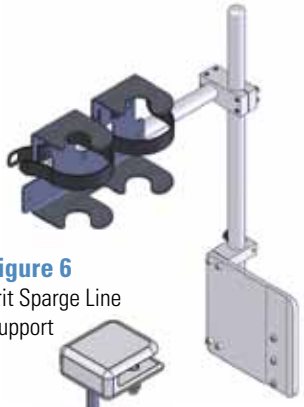


Figure 5
Filter Bracket Adapter (for use with resistive heater S.U.B.)

Figure 6
Frit Sparge Line Support

Single-Use Bioreactor (S.U.B.) First Time Operator—Recommended Parts List

Available Parts (consumables sufficient for three complete cell culture runs)		
Part Number	**Description**	**Quantity**
SV50174 (1000 L)	S.U.B. Hardware System (standard)	1
SH30774.05	S.U.B. BPC (standard)	3
SH30720.01	Bioreactor Probe Assembly (non-sterile for use in autoclave)	12
SV20664.03	Heavy Duty Tubing Clamp (10 pack)	1
SV50177.01	Autoclave Tray for Autoclaving Probe Kits	2
SV20750.01	S.U.B. Temperature Port (used to verify RTD calibration)	1
SH30845.02	Sterile Sampling Manifold with Luer Locks (10 pack)	3
Auxiliary Components Supporting The Single-Use Bioreactor		
Description	**Purpose**	**Quantity**
Bioreactor control system	Necessary for regulation of gas pressure and flow rate control for DO and pH set points	1
DO probe	Autoclavable Probe (13 mm X 13.5PG thread w/ 195-235 mm insertion length)	1
pH probe	Autoclavable Probe (13 mm X 13.5PG thread w/ 195-235 mm insertion length)	1
Sterile/Aseptic Connection Method	Tubing Welder (Terumo or Wave), Steam In Place (SIP) Sterilizer, or Laminar Flow Hood	1
Peristaltic Pump	Used for fluid transfer between line sets and containers	1
Temperature Control Unit (TCU)	Necessary for water jacket temperature control (not provided)	1

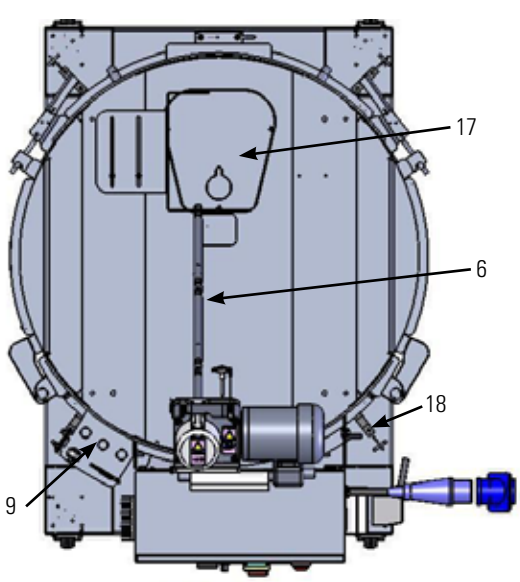
Hardware Features

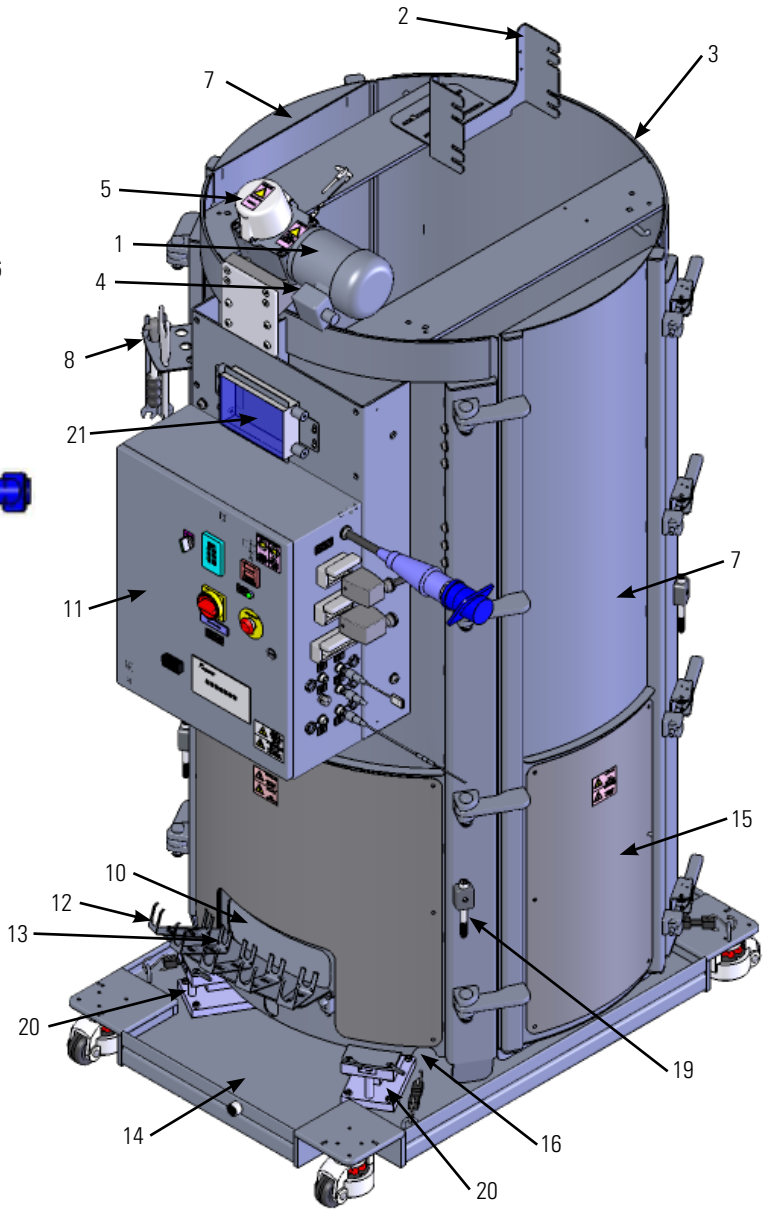
1000 L with Electric Resistive Heater:

The stainless steel outer support container contains the following features:

1. Mixer motor
2. Exhaust vent filter holder
3. Stainless steel outer support container
4. Bearing port receiver with clamp
5. Mixing assembly with shield
6. Drive shaft
7. Doors (2)
8. Standard tool set
9. Drive shaft storage holder
10. Probe access window
11. Control panel
12. Probe holder
13. Probe shelf
14. Platform with swivel casters and leveling pads
15. Resistive heater with shield (5)
16. Bottom cut outs for BPC alignment
17. Sparge access window
18. Stretch hooks
19. Load cell calibration mount
20. Load cells (3)
21. Load cell summing block

Top View





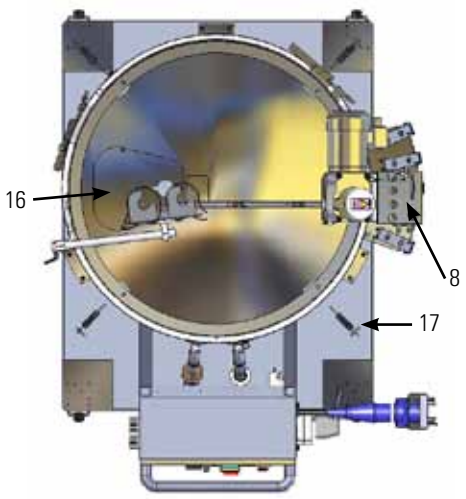
Hardware Features

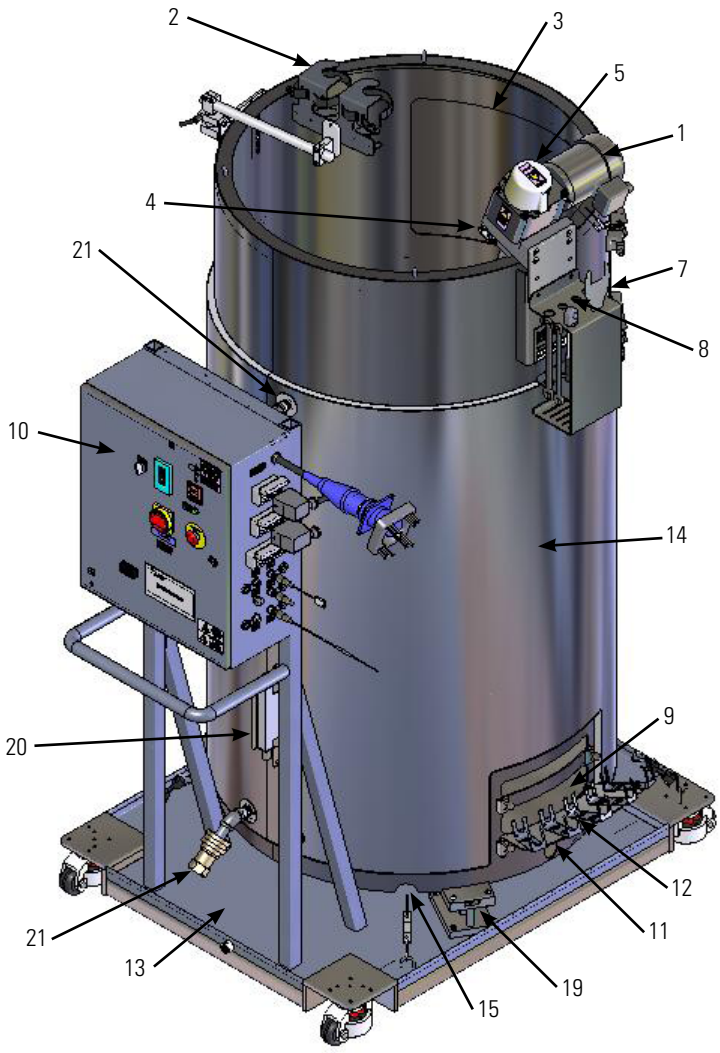
1000 L with Water Jacket:

The stainless steel outer support container contains the following features:

1. Mixer motor
2. Exhaust vent filter holder
3. Stainless steel outer support container
4. Bearing port receiver with clamp
5. Mixing assembly with shield
6. Drive shaft (not shown)
7. Standard tool set
8. Drive shaft storage holder
9. Probe access window
10. Control panel
11. Probe holder
12. Probe shelf
13. Platform with swivel casters and leveling pads
14. Water jacket
15. Bottom cut outs for BPC alignment
16. Sparge access window
17. Stretch hooks
18. Load cell calibration mount (not shown)
19. Load cells (3)
20. Load cell summing block
21. Jacket quick connect couplings

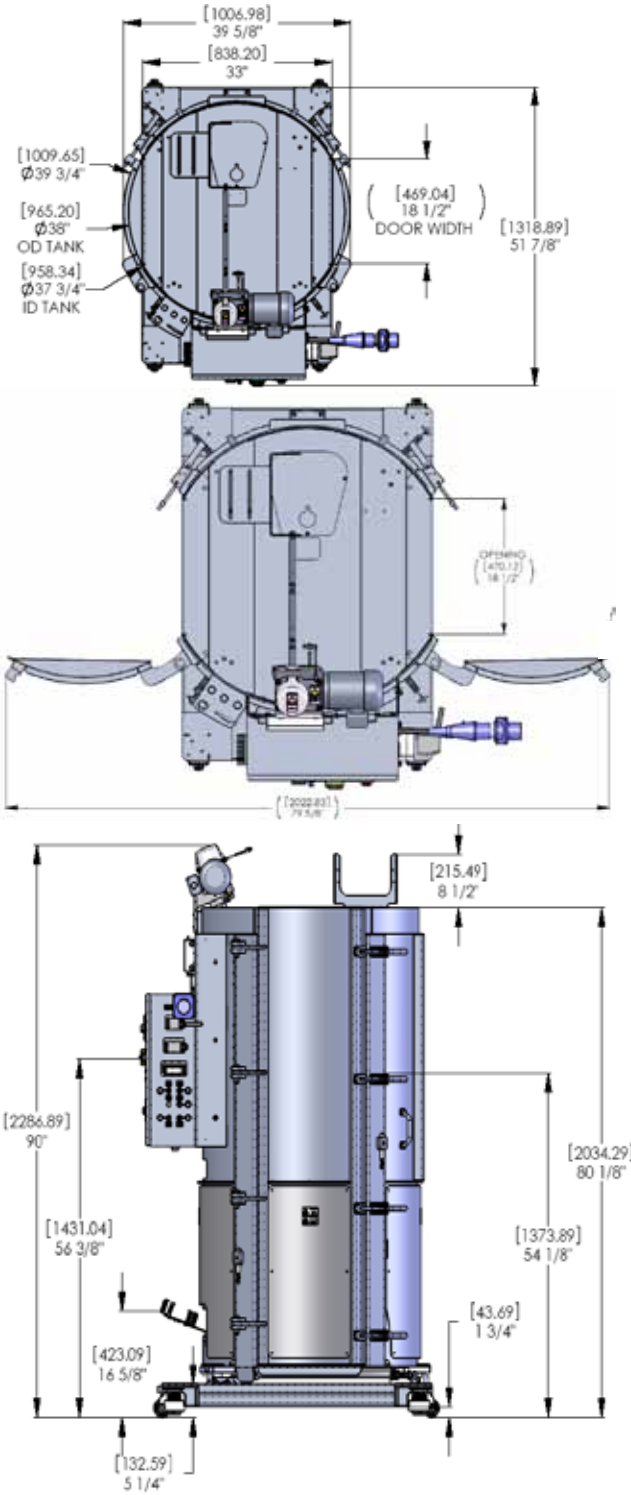
Top View



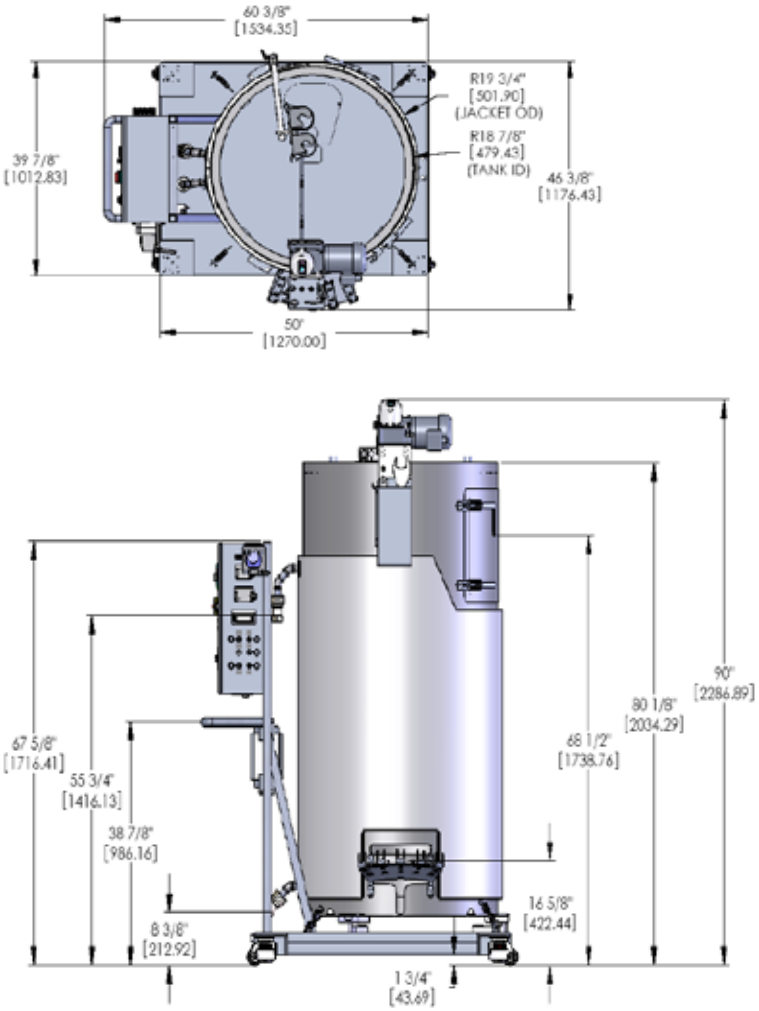


Outer Support Container (units in inches [mm])

1000 L S.U.B. Electric Resistive Heater:



1000 L S.U.B. Water Jacket:



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Thermo SCIENTIFIC

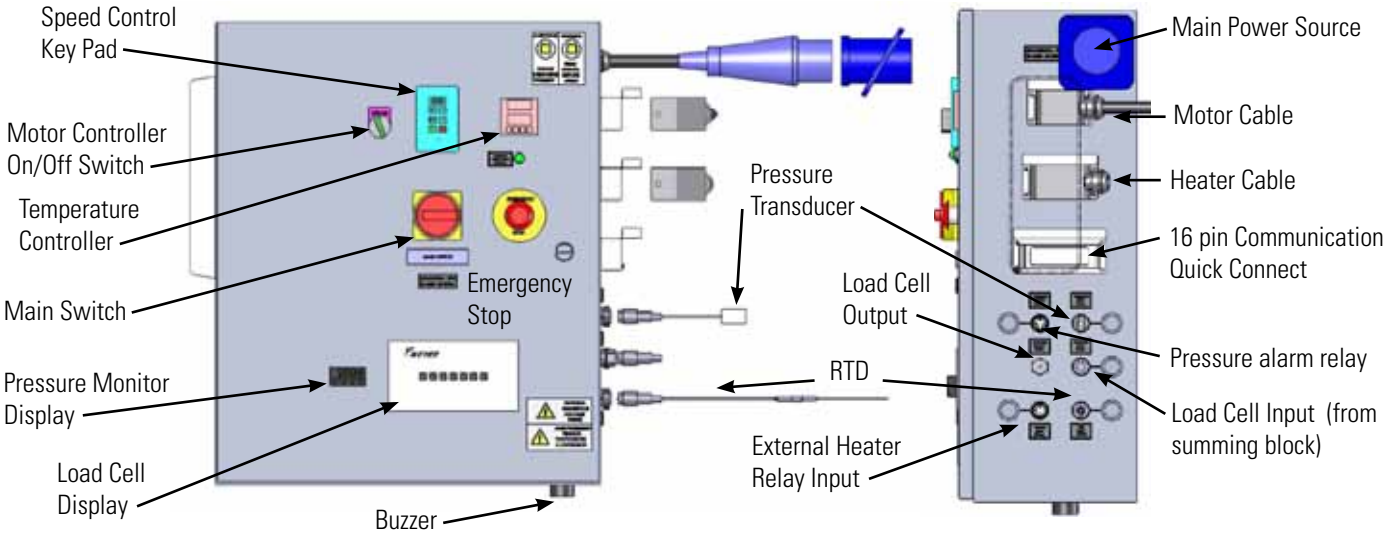
3.5.2 1000 L Hardware Specifications Electric Resistive Heater

Reactor Geometry	Rated Liquid Working Volume	(1000 liter)
	Minimum Liquid Working Volume	(500 liter)
	Total Reactor Volume	(1320 liter)
	BPC Chamber Diameter	37.75" (95.9 cm)
	BPC Chamber Shoulder Height	79" (200.7 cm)
	Liquid Height @ Rated Working Volume	56" (142.2 cm)
	Fluid Geometry @ Working Volume (height/diameter) Ratio	1.5
	Overall Reactor Geometry (height/diameter) Ratio	1.9
	Tank Baffles	no
Impeller	Impeller (quantity X blade count)	1 X 3
	Impeller Scaling (impeller diameter/tank diameter)	1/3
	Impeller Blade Pitch (angle)	45°
	Impeller Diameter	12.625" (32.1 cm)
	Impeller - Calculated Power Number (N)	2.1
Agitation Parameters	Maximum Mixing Rate (revolutions per minute)	20-110 rpm
	Nominal Agitation Rating - Power/Volume Ratio	0.1 hp/1000 gal (19.7 W/1000 liter)
	Nominal Agitation (revolutions per minute)	87 rpm
	Nominal Tip Speed	287.6 ft/min (146.1 cm/s)
	Counterclockwise Mixing Flow Direction	down-pumping
	Agitation Shaft Resolved Angle	19.6°
	Agitation Shaft Centerline Offset	2.00" (5.08 cm)
	Overall Drive Shaft Length	66" (167.6 cm)
	Operational Drive Shaft Length	60" (152.4 cm)
	Drive Shaft Diameter	0.75" (1.91 cm)
	Drive Shaft Poly-Sheath Outside Diameter	1.38" (3.51 cm)
	Impeller Clearance from Tank Bottom	12.625" (32.1 cm)
Motor	Agitation Motor Drive (type, voltage, phase)	Induction, 208 VAC, three
	Motor Power Rating	0.5 hp (372.8 kW)
	Motor Torque Rating	245 in-lbs (27.7 Nm)
	Gear Reduction	15:1
	Programmable VFD, Remote Panel Interface, Power Fault Auto-Restart	standard
	Motor Communication Methods (for external controller)	0-10V, 4-20 mA, ModBus
Temp Control	Programmable PID Temperature Controller	standard
	RTD or Thermocouple, 1/8" (3.18 mm) OD	RTD: Pt-100 (standard)
	Heater Style	resistive
	Solid State Relay (discrete voltage signal)	24-240V AC/DC
	Heater Power Rating	5000 W
	Approximate Liquid Heat-Up Time: (2-37°C)	12 hours
Support Container	Overall Width	40" (101.6 cm)
	Overall Length	48" (121.9 cm)
	Overall Height	84" (213.4 cm)
	Dry Skid Weight (mass)	600 lbs (272 kg)
	Wet Skid Weight—Rated Working Volume (mass)	2805 lbs (1272 kg)
General	Electrical Power Supply Requirement (voltage, phase, amp)	280/240 VAC, single, 30 A
	Operating Temperature (with heater)	Ambient to 40 +/- 0.1 °C (104 +/- 0.2 °F)
	Validated System Reliability (minimum)	0.9 @ 90%

3.5.3 1000 L Hardware Specifications Water Jacket

Reactor Geometry	Rated Liquid Working Volume	(1000 liter)
	Minimum Liquid Working Volume	(500 liter)
	Total Reactor Volume	(1320 liter)
	BPC Chamber Diameter	37.75" (95.9 cm)
	BPC Chamber Shoulder Height	79" (200.7 cm)
	Liquid Height @ Rated Working Volume	56" (142.2 cm)
	Fluid Geometry @ Working Volume (height/diameter) Ratio	1.5
	Overall Reactor Geometry (height/diameter) Ratio	1.9
	Tank Baffles	no
Impeller	Impeller (quantity X blade count)	1 X 3
	Impeller Scaling (impeller diameter/tank diameter)	1/3
	Impeller Blade Pitch (angle)	45°
	Impeller Diameter	12.625" (32.1 cm)
	Impeller - Calculated Power Number (N)	2.1
Agitation Parameters	Maximum Mixing Rate (revolutions per minute)	20-110 rpm
	Nominal Agitation Rating - Power/Volume Ratio	0.1 hp/1000 gal (19.7 W/1000 liter)
	Nominal Agitation (revolutions per minute)	87 rpm
	Nominal Tip Speed	287.6 ft/min (146.1 cm/s)
	Counterclockwise Mixing Flow Direction	down-pumping
	Agitation Shaft Resolved Angle	19.6°
	Agitation Shaft Centerline Offset	2.0" (5.08 cm)
	Overall Drive Shaft Length	66" (167.6 cm)
	Operational Drive Shaft Length	60" (152.4 cm)
	Drive Shaft Diameter	0.75" (1.91 cm)
	Drive Shaft Poly-Sheath Outside Diameter	1.38" (3.51 cm)
	Impeller Clearance from Tank Bottom	12.625" (32.1 cm)
Motor	Agitation Motor Drive (type, voltage, phase)	Induction, 208 VAC, three
	Motor Power Rating	0.5 hp (372.8 kW)
	Motor Torque Rating	245 in-lbs (27.7 Nm)
	Gear Reduction	15:1
	Programmable VFD, Remote Panel Interface, Power Fault Auto-Restart	standard
	Motor Communication Methods (for external controller)	0-10V, 4-20 mA, ModBus
Temp Control	Jacket type	Low profile Stainless Steel Laser Dimpled Jacket with Exterior Insulation Shield
	Jacket area: full/half volume (ft^2)	35.56/14.87
	Jacket Volume (L)	2.75 liters
	Jacket Flow Rate at 50 psi	21 liters/min
	RTD or Thermocouple, 1/8" (3.18 mm) OD	RTD: Pt-100 (standard)
	Process Connection	3/4" MNPT nipple with Hansen quick connect check valves
	Nominal heating/cooling load (W)	1000
	Nominal heating/cooling time [5-37C] (hr)	8
Support Container	Overall Width	40" (101.6 cm)
	Overall Length	48" (121.9 cm)
	Overall Height	84" (213.4 cm)
	Dry Skid Weight (mass)	1138 lbs (516.2 kg)
	Wet Skid Weight—Rated Working Volume (mass)	3342.6 lbs (1516.2kg)
General	Electrical Power Supply Requirement (voltage, phase, amp)	120/240 VAC, single, 30 A
	Operating Temperature (with heater)	Ambient to 40 +/- 0.1 °C (104 +/- 0.2 °F)
	Validated System Reliability (minimum)	0.9 @ 90%

3.5.4 1000 L Control Panel Layout



3.6 2000 L Single-Use Bioreactor

Data Sheet 066 Rev 1

Thermo Scientific HyClone Single-Use Bioreactor (S.U.B.) 2000 L

The Thermo Scientific HyClone Single-Use Bioreactor (S.U.B.) is the leading single-use alternative to conventional stirred tank bioreactors for animal and insect cell culture. The current range includes units with maximum working volumes of 50, 100, 250, 500, 1000 and 2000 L. The S.U.B. is now available with new optimized standard BioProcess Containers with improved dual sparge capability. Open pipe and frit sparging systems are now included to provide a wider range of operating conditions.

Overview:

The HyClone® S.U.B. provides all the advantages of single-use bioprocessing without having to buy a complete new bioreactor system. The critical design parameters of the S.U.B., such as height to diameter ratios, mixer design and location and typical control system interfaces, have been maintained.

The S.U.B. BioProcess Container™ (BPC®) is supplied sterilized by irradiation and therefore does not require any facility hook-ups for sterilization or cleaning. A key element to the single-use design is the plastic (Kynar) impeller with a bearing/seal assembly linked to an external mixer drive.

2000 L Water Jacket S.U.B.

This document covers S.U.B. systems with a maximum working volume of 2000 L and the new optimized standard S.U.B.s with dual sparge capability which provides for a wide range of k_La values, plus better pH control and lower foaming than the original disk sparger.

The S.U.B. system consists of the following components:

1. Outer Support Container—with a mixer drive complete with control unit, and a water jacketed tank.
2. Single-Use Bioreactor BPC—complete with agitator assembly, spargers, overlay and exhaust filter ports, plus ports for integration of sensor probes and line sets for media and supplement addition and sampling. The S.U.B. BPC is supplied sterile and ready-to-use.
3. Drive Shaft—inserted into the S.U.B. BPC through the mixing drive motor and locked into the disposable agitator assembly.
4. Process Controls—agitation control is integrated into the S.U.B., but additional temperature, pH, and dissolved oxygen (DO) controls must be supplied.
5. Condenser System—auxiliary system providing protection against vent filter blockage. Guidance data regarding when to use, as well as further information, are found in the Condenser System data sheet.

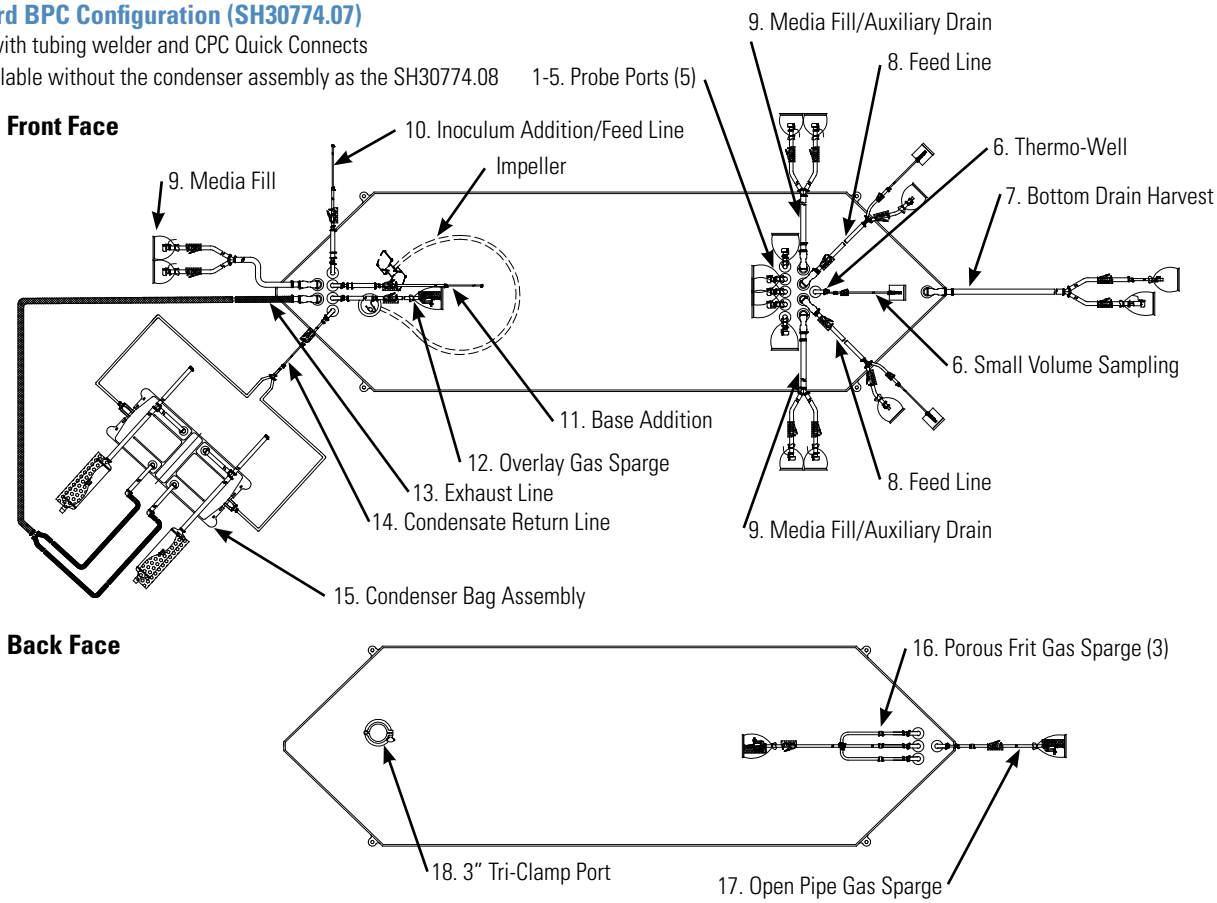
Item	2000 L Water Jacket
Rated Liquid Working Volume	2000 L
Minimum Liquid Working Volume	1000 L
Total Reactor Volume (Liquid & Gas)	2575 L
BPC Chamber Diameter	47" (119.4 cm)
BPC Chamber Shoulder Height	90.5" (229.9 cm)
Liquid Height @ Rated Working Volume	70.35" (178.7 cm)
Overall Reactor Geometry (height/diameter ratio)	1.9:1
Fluid Geometry @ Working Volume (height/diameter ratio)	1.5:1
Impeller (quantity x blade count)	1 x 3
Impeller Diameter	15.67" (39.8 cm)
pH & DO Probe— Autoclavable Type (Applisens, Broadley James, Metler Toledo)	12 mm diameter x 215-235 mm insertion length x 13.5 PG thread
Hold-Up Volume	< 4 L
Electrical Power Supply Requirement (voltage, phase, amp)	208-240 VAC, single, 30 A
Overall Width	52" (132.1 cm)
Overall Length	54" (137.2 cm)
Overall Height	126.4" (321.1 cm)
S.U.B. Recommended Operating Parameters	
Operating Temperature Range	Ambient to 40 +/- 0.1°C (104 +/- 0.2°F)
Motor Speed	20-75 rpm
Volume Range	1000-2000 L
Maximum Bag Pressure	0.5 psi (0.03 bar)
Continuous Operating Time	21 days*

*Mixing time at nominal volume only.

Standard BPC Configuration (SH30774.07)

For use with tubing welder and CPC Quick Connects

Also available without the condenser assembly as the SH30774.08



Standard BPC Configuration (CX5-14 Film)

For use with tubing welder and CPC Quick Connects

Line	Description	Tubing Set (ID X OD X Length)	End Treatment
1-5	Probe Ports (5)	1/2" (12.7 mm) Tube ports	Pall® Kleenpak™ aseptic connectors (Female)
6	Thermo-Well/ Small Volume Sample	Thermo-Well Adapter for 1/4" (6.4 mm) Diameter. 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex® X 24" (61 cm)	SterilEnz® Pouch with injection site assembly
7	Bottom Drain Harvest	3/4" (19.1 mm) ID X 1" (25.4 mm) OD C-Flex X 48" (122 cm) splits to 1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 24" 61 cm) reduced to 1/4" (6.4 mm) ID X 3/8" (9.5 mm) OD C-Flex X 12" (30 cm) and 1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 24" 61 cm)	1/4" MPC Insert and Pall Kleenpak (Male)
8	Feed Line	1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 4" (10 cm) splits to 1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 10" (25 cm) and 1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 10" (25 cm)	SterilEnz Pouch with injection site assembly and 3/8" MPC Body
9	Media Fill	3/4" (19.1 mm) ID X 1" (25.4 mm) OD C-Flex X 84" (213 cm) splits to 1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 24" (61 cm) and 1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 24" (61 cm)	Pall Kleenpak aseptic connectors (Female)
10	Inoculum Addition/ Feed Line	1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 3" (8 cm) reduced to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 6" (15 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 84" (213 cm)	Plugged
11	Base Addition	1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 3" (8 cm) reduced to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 84" (213 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm)	Plugged
12	Overlay Gas Sparge	1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 4" (10 cm) reduced to 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 84" (213 cm)	Kleenpak Emflon II Capsule and Pressure transducer
13	Exhaust Line	Condenser Bag Assembly	
14	Condensate Return Line	Condenser Bag Assembly	
15	Condenser Bag Assembly	Condenser Bag Assembly	
16	Porous frit gas sparge 12 mm dia (25 µm pores)	(3x) 12 mm PDVF Porous Sparge Inserts connected to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 6" (15 cm) converge to one 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 72" (183 cm)	Kleenpak Emflon II Capsule
17	Open Pipe Gas Sparge	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 72" (183 cm) reduced to Check Valve and 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 72" (183 cm)	Kleenpak Emflon II Capsule
18	3" Tri-Clamp Port	NA	Gasket end cap, and clamp

Ordering Information for Standard BPC Products

Custom BPC Options:

Category	Options/Capability	Remarks
Tubing Type	C Flex, platinum cured silicone, PVC, Pharmed®, PharmaPure®	More information in selection guide of BPC catalog
Tubing Size	Specific lengths of 1/8" ID to 1" ID	ID limitations due to port size
Connectors	Luers, CPC Quick Connects, SIP connectors, Triclamp, Kleenpak, Lynx®, SmartSite®, Clave®, Lynx steam thru, CPC Steam Thru, Gore steam valve, Gore Mini TC, BioQuate (GE), PAW SterilEnz®, end plug, etc.	Refer to selection guide in BPC catalog for further information by connection type. **Note:** Only option for probe port connections is Kleenpak.
Kleenpak (i.e., probe) ports	Additional ports: second row of 4 for 50 L to 250 L S.U.Bs.; second row of 5 for 500 L and 1000 L S.U.B.s	
Disposable sensors	Pressure sensor: Pendotech for 50 L to 500 L S.U.B. (comes standard on 1000 L and 2000 L) DO, pH, Pressure – Finesse DO and pH – PreSens Availability of various other disposable sensors currently pending.	
Addition of ports/lines (other than 2nd row of probe ports)	Limited engineer-to-order customization possible such as additional media lines and vent filter lines. Requires economic justification.	Dependent on location in bag and compatibility with hardware
Port sizes	Limited customization possible as engineer-to-order with justification.	Dependent on location in bag and fit with hardware (e.g., 1" ID port on harvest line)
Re-arrangement of lines on existing ports	Limited customization possible, e.g., moving sample/tempwell port to a probe tube port, or swapping overlay inlet line with supplement line.	Dependent on location in bag and fit with hardware
Sparger	Dual sparger (open pipe plus porous frit) standard. Can do an engineer-to-order for one or the other alone. Make-to-order bags will be built around standard dual sparger chamber.	
Dip tube lines	Limited customization possible. Suggested use through 1" port, so this is engineer-to-order. Otherwise must use ferrule approach.	Length cannot interfere with impeller and shaft. Typical is 10" or shorter.
Overlay and Sparge Line Filters	Can use disposable (capsule) filter other than standard hydrophobic vent filter with Emflon II.	
Vent Filters	Standard is Pall Kleenpak 0.2 micron exhaust vent filter.	**Note:** Vent filter heater configuration restricts options
Vent Filter Tubing Length	Extended filter height above the S.U.B. bag is make-to-order.	Must be compatible with a vent filter bracket option
Filters on Media and Supplement Inlets	Choice of filters for inlets used to sterile filter incoming media or supplements.	

Please Note: Not all options are available for all ports. No customization of port type and location, chamber dimensions or mixing assembly is possible. For additional information, please see the Selection Guides in the S.U.B. BPC Catalog.

Presentation (as dry BPC systems):

Outer Packaging	Supplied 'flat-packed' Two polyethylene outer layers
Label	Description Product code Lot number Expiry date on outer packaging and shipping container
Sterilization	Irradiation (25 to 40 kGy) inside outer packaging
Shipping Container	Durable cardboard carton
Documentation	Certificate of Analysis provided with each lot for each delivery

Water Jacket:

Part Number	Description	
SV50223.11	2000 L S.U.B., Modbus Plus Load Cell Interface (240 VAC)	Includes: 304 stainless steel outer support container, variable speed agitation controller, motor, drive assembly with 4 segment drive shaft, RTD sensor, integrated water jacket, three load cells with summing block/display, BPC pressure monitor, probe support system, and standard tool set.
SV50223.12	2000 L S.U.B., Allen-Bradley Load Cell Interface (240 VAC)	
SV50223.13	2000 L S.U.B., Analog Output Load Cell Interface (240 VAC)	
SV50223.14	2000 L S.U.B., Profibus Load Cell Interface (240 VAC)	
SV50223.15	2000 L S.U.B., DeviceNet Load Cell Interface (240 VAC)	

Custom Options

Custom Hardware Options

For stainless steel capabilities, please contact your sales representative for HyClone products for more information.

Accessories

Part Number	Description	
SH30720.01	Bioreactor Probe Assembly (non-sterile)	Used to package the pH and DO probes (not supplied) for sterilization and to aseptically connect them to the S.U.B. BPC. See Figure 1.
SV20664.01	Heavy Duty Tubing Clamp	Reusable tubing clamp used on probe ports when connecting probe assemblies.
SV20664.02	Heavy Duty Tubing Clamp (4 pack of SV20664.01)	
SV20664.03	Heavy Duty Tubing Clamp (10 pack of SV20664.01)	
SV20750.01	S.U.B. Temperature/Sample Port	Used for RTD calibration/validation.
SV50177.01	Autoclave Tray for Probe Kits (stainless steel)	Support tray which allows the probes to be safely autoclaved. See Figure 2.
SH30845.01	Sterile Sampling Manifold with luer lock (individual)	Available for aseptic luer connection or weld onto the sample line to take sample sets.
SH30845.02	Sterile Sampling Manifold with luer lock (10 pack)	
SV50177.65	Frit Sparge Line Support	Recommended to maintain the frit sparge in a vertical position.
SV50177.258	Elevated Dual Filter Bracket	For use on tank when not using condenser system. See Figure 3.
SV30135.01	Mobile Stairs	Facilitate access to top of bioreactor.
SV50177.23	Hanging Probe Clips	Support probes while inserted into bioreactor.
SV50191.01-09	Vent Filter Heater and Cord Options	For use with exhaust filters when not using condenser system.

Figure 1
Bioreactor Probe Assembly

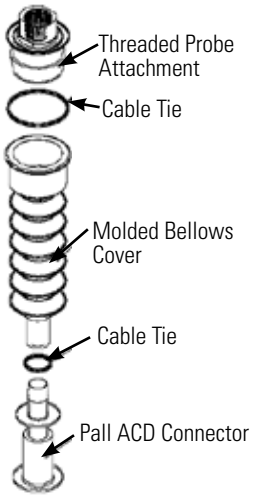
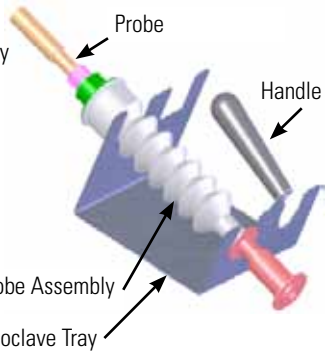


Figure 2
Autoclave Tray for Probe Kits



Additional information on autoclave tray::

- Fabricated from stainless steel
- Plastic carry handle for easy transport right out of the autoclave
- Positions probes on 15% incline for greater probe/membrane longevity
- Will restrain probe bellows from collapsing during sterilization
- Probe holder accommodates two probes

Figure 3
Elevated Dual Filter Brackets and Filter Heater Supports

Figure 4
Frit Sparge Line Support

Single-Use Bioreactor (S.U.B.) First Time Operator—Recommended Parts List

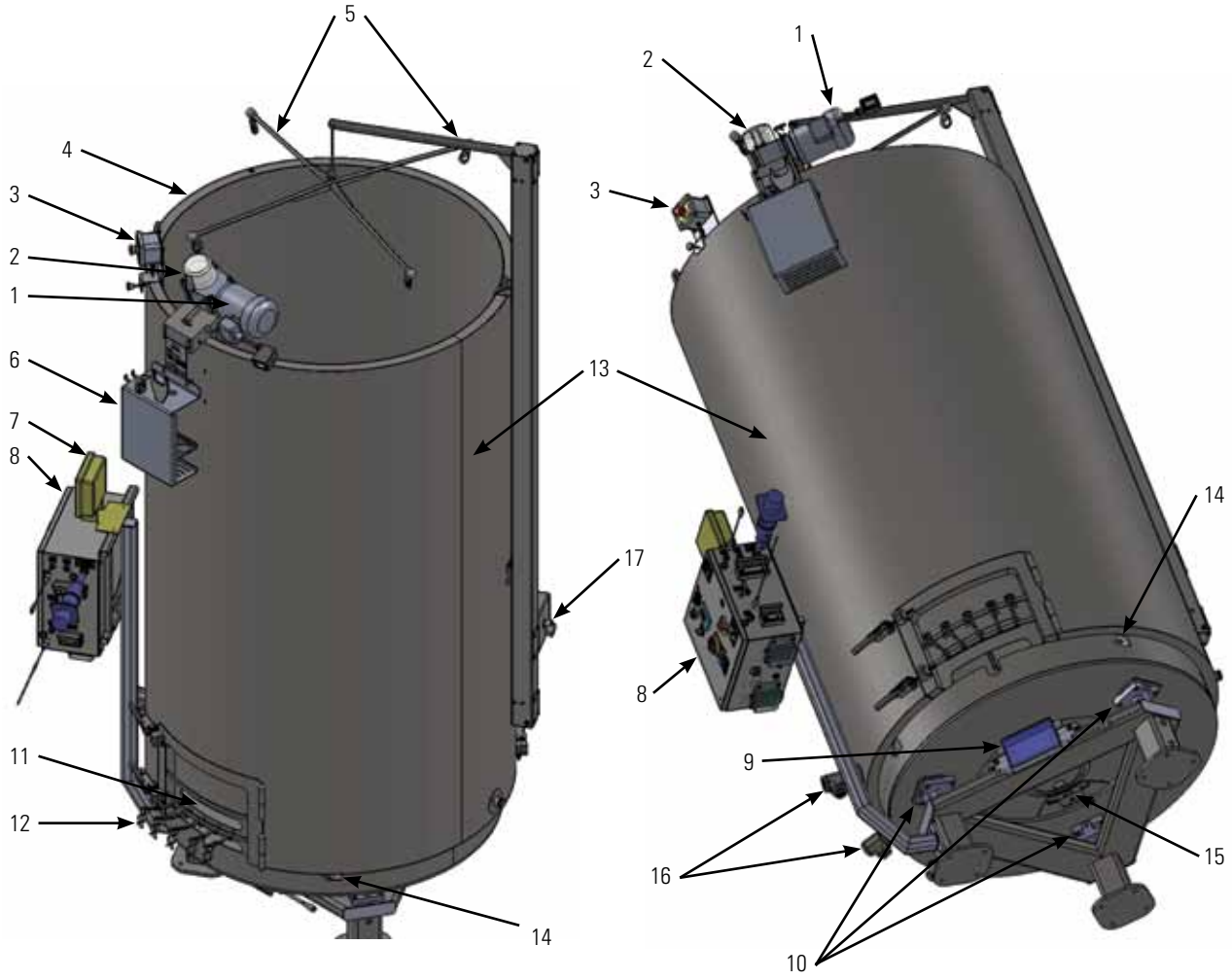
Available Parts (consumables sufficient for three complete cell culture runs)		
Part Number	**Description**	**Quantity**
SV50223 (2000 L)	S.U.B. Hardware System (standard)	1
SH30774.07 or SH30774.08	S.U.B. BPC (standard) with or without condenser bag assembly	3
SH30720.01	Bioreactor Probe Assembly (non-sterile for use in autoclave)	12
SV20664.03	Heavy Duty Tubing Clamp (10 pack)	1
SV50177.01	Autoclave Tray for Autoclaving Probe Kits	2
SV20750.01	S.U.B. Temperature Port (used to verify RTD calibration)	1
SH30845.02	Sterile Sampling Manifold with Luer Locks (10 pack)	3
Auxiliary Components Supporting The Single-Use Bioreactor		
Description	**Purpose**	**Quantity**
Bioreactor control system	Necessary for regulation of gas pressure and flow rate control for DO and pH set points	1
DO probe	Autoclavable Probe (13 mm X 13.5PG thread w/ 195-235 mm insertion length)	1
pH probe	Autoclavable Probe (13 mm X 13.5PG thread w/ 195-235 mm insertion length)	1
Sterile/Aseptic Connection Method	Tubing Welder (Terumo or Wave), Steam In Place (SIP) Sterilizer, or Laminar Flow Hood	1
Peristaltic Pump	Used for fluid transfer between line sets and containers	1
Temperature Control Unit (TCU)	Necessary for water jacket temperature control	1

Hardware Features

2000 L with Water Jacket:

The stainless steel outer support container contains the following features:

1. Mixer motor
2. Mixing assembly with shield
3. External E-Stop assembly
4. Stainless steel outer support container
5. Bag lift assembly
6. Standard tool set
7. Load cell display
8. Control panel
9. Load cell summing block
10. Load cell (3)
11. Probe access window
12. Probe clips
13. Water jacket
14. Bottom cut outs for BPC alignment
15. Sparge access plate
16. Jacket quick connect couplings
17. Pneumatic bag lift control

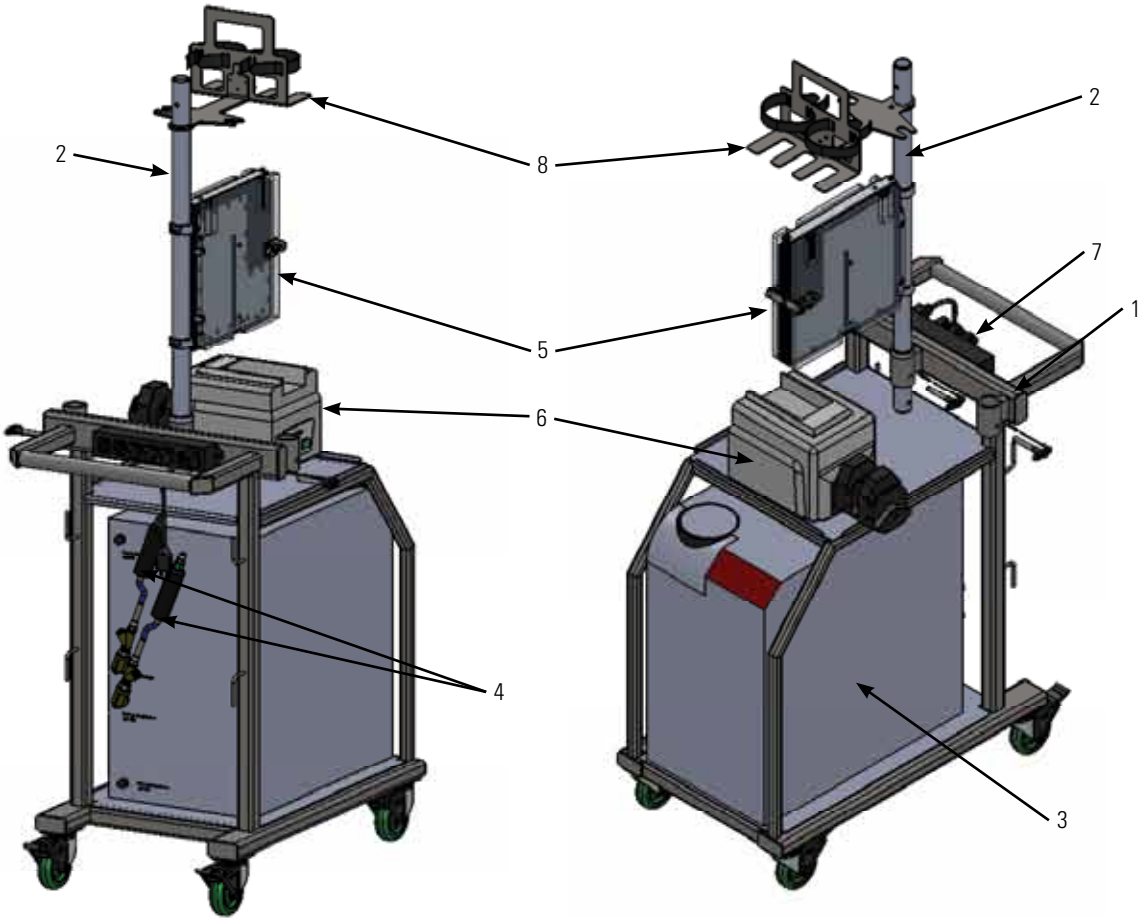


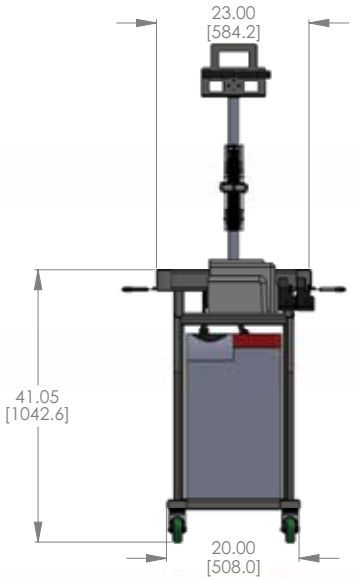
Hardware Features

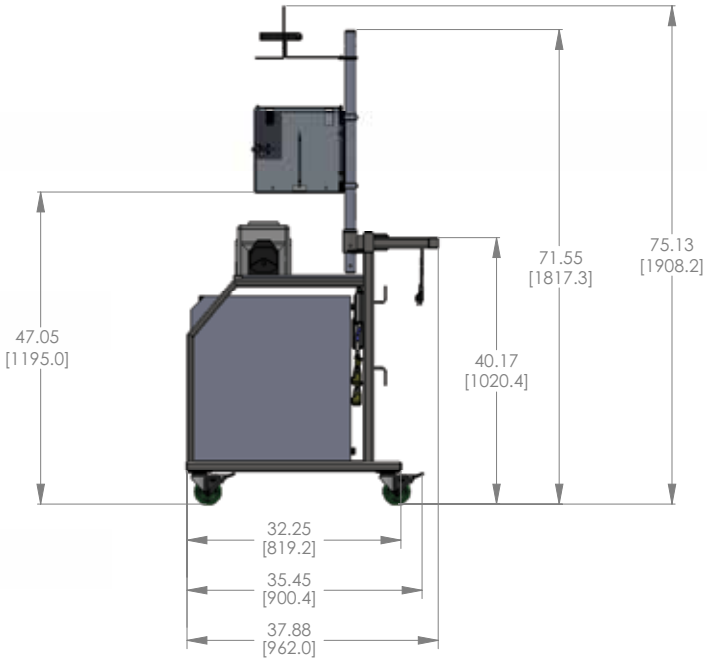
Condenser System:

The Condenser System contains the following features:

1. Condenser cart assembly
2. Condenser post/filter bracket assembly
3. Chiller (temperature control unit-TCU)
4. Chiller line assembly
5. Chiller Plate
6. Pump assembly
7. Electrical power strip
8. Filter brackets

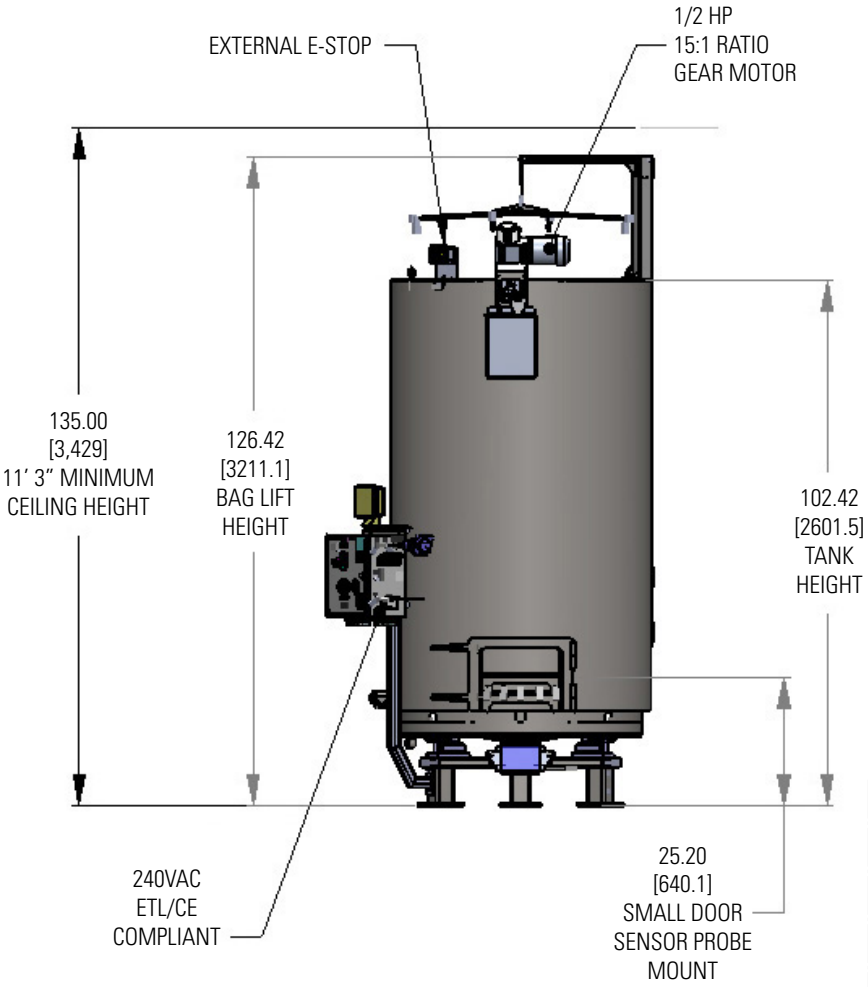


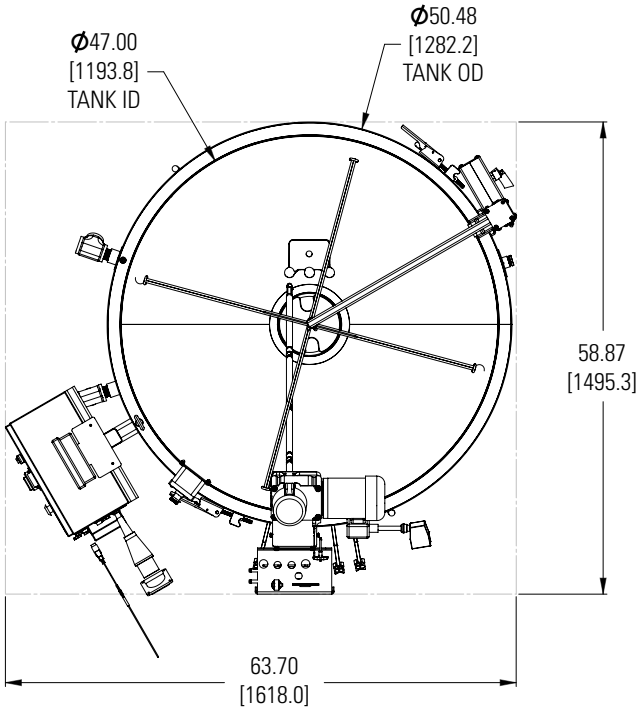




Outer Support Container (units in inches [mm])

2000 L S.U.B. Water Jacket:





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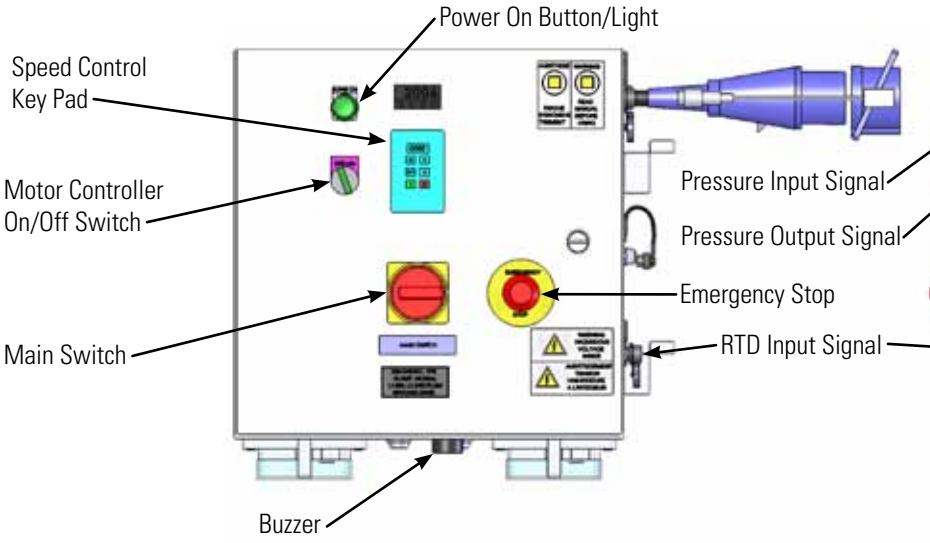
Thermo SCIENTIFIC

3.6.2 2000 L Hardware Specifications Water Jacket

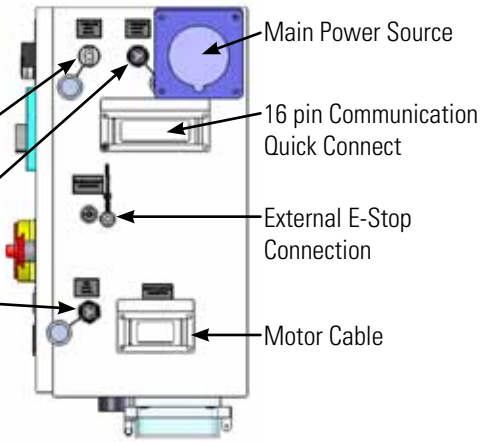
Reactor Geometry	Rated Liquid Working Volume	2000 liter
	Minimum Liquid Working Volume	1000 liter
	Total Reactor Volume	2575 liter
	BPC Chamber Diameter	47" (119.4 cm)
	BPC Chamber Shoulder Height	90.5" (229.9 cm)
	Liquid Height @ Rated Working Volume	70.35" (178.7 cm)
	Fluid Geometry @ Working Volume (height/diameter) Ratio	1.5
	Overall Reactor Geometry (height/diameter) Ratio	1.9
	Tank Baffles	no
Impeller	Impeller (quantity X blade count)	1 X 3
	Impeller Scaling (impeller diameter/tank diameter)	1/3
	Impeller Blade Pitch (angle)	45°
	Impeller Diameter	15.67" (39.8 cm)
	Impeller - Calculated Power Number (N)	2.1
Agitation Parameters	Maximum Mixing Rate (revolutions per minute)	20-75 rpm
	Nominal Agitation Rating - Power/Volume Ratio	0.1 hp/1000 gal (19.7 W/1000 liter)
	Nominal Agitation (revolutions per minute)	75 rpm
	Nominal Tip Speed	305 ft/min (154.9 cm/s)
	Counterclockwise Mixing Flow Direction	down-pumping
	Agitation Shaft Resolved Angle	19.6°
	Agitation Shaft Centerline Offset	2.63" (6.7 cm)
	Overall Drive Shaft Length	82" (208.3 cm)
	Operational Drive Shaft Length	72.5" (184.2 cm)
	Drive Shaft Diameter	0.75" (1.91 cm)
	Drive Shaft Poly-Sheath Outside Diameter	1.38" (3.51 cm)
	Impeller Clearance from Tank Bottom	15.67" (39.8 cm)
Motor	Agitation Motor Drive (type, voltage, phase)	Induction, 208 VAC, three
	Motor Power Rating	0.5 hp (372.8 kW)
	Motor Torque Rating	245 in-lbs (27.7 Nm)
	Gear Reduction	15:1
	Programmable VFD, Remote Panel Interface, Power Fault Auto-Restart	standard
	Motor Communication Methods (for external controller)	0-10V, 4-20 mA, ModBus
Temp Control	Jacket type	3/8" dimple hand-weld
	Jacket area: actual/effective	side jacket (8595 in^2/6833 in^2) bottom jacket (1066 in^2/927 in^2)
	Jacket Volume	side jacket (37 L), bottom jacket (7 L)
	Jacket Flow Rate at 50 psi	75 liters/min
	RTD or Thermocouple, 1/8" (3.18 mm) OD	RTD: Pt-100 (standard)
	Process Connection	1" mNPT Threaded Nipple Provided w/ Hansen Quick Connect Check Valves
	Nominal heating/cooling load	10 watts/liter
	Nominal heating/cooling time [5-37C]	6 hrs
Support Container	Overall Width	52" (132.1 cm)
	Overall Length	54" (137.2 cm)
	Overall Height	126.4" (321.1 cm)
	Dry Skid Weight (mass)	1800 lbs (816 kg)
	Wet Skid Weight—Rated Working Volume (mass)	6200 lbs (2812 kg)
General	Electrical Power Supply Requirement (voltage, phase, amp)	208-230 VAC, single, 30 A
	Operating Temperature (with heater)	Ambient to 40 +/- 0.1 °C (104 +/- 0.2 °F)
	Validated System Reliability (minimum)	0.9 @ 90%

3.6.3 2000 L Control Panel Layout

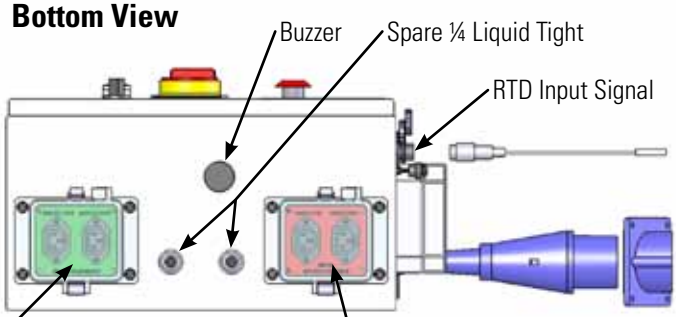
Front View



Side View

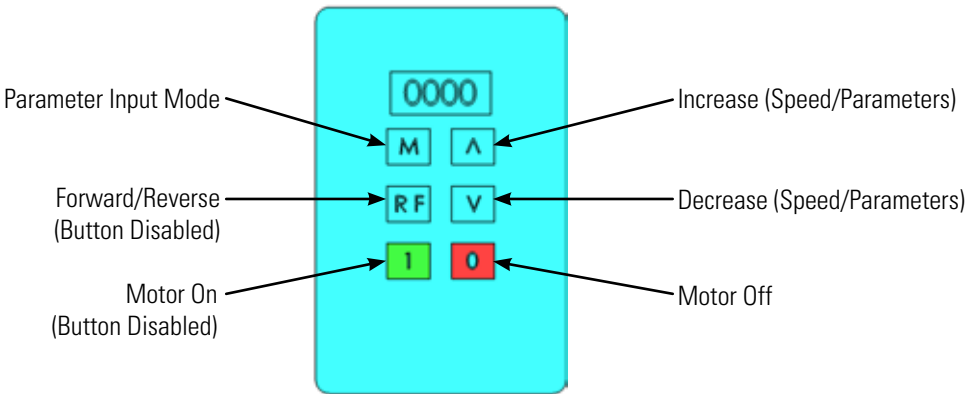


Bottom View



Continuous Power
This outlet is used for devices that should not be turned off during an E-stop. Examples are recording devices, sensors, controllers, etc. The max for each receptacle is ½ amps.

Emergency Shut-off Power
This outlet is used for devices that should be turned off when an operator activates an E-stop. Examples are pumps, motors, or any device that could potentially harm an operator or ruin a batch during an E-stop. The max for each receptacle is 2 amps.



3.7 Standard BioProcess Containers with Disk Sparge Systems Data Sheet

Data Sheet 062 Rev 1

Thermo Scientific HyClone Single-Use Bioreactor (S.U.B.)

Standard BioProcess Containers with Disk Sparge System

The Thermo Scientific HyClone Single-Use Bioreactor (S.U.B.) is the leading single-use alternative to conventional stirred tank bioreactors for animal and insect cell culture. The current range includes units with maximum working volumes of 50, 100, 250, 500, 1000 and 2000 L. The S.U.B. is now available with new optimized standard BioProcess Containers with improved, dual sparge capability. Open pipe and frit sparging systems are now included to provide a wider range of operating conditions. The 2000 L S.U.B. BPC is not available with the Disk Spage System.

Overview:

The HyClone® S.U.B. provides all the advantages of single-use bioprocessing without having to buy a complete new bioreactor system. The critical design parameters of the S.U.B., such as height to diameter ratios, mixer design and location and typical control system interfaces, have been maintained.

The S.U.B. BioProcess Container™ (BPC®) is supplied sterilized by irradiation and therefore does not require any facility hook-ups for sterilization or cleaning. A key element to the single-use design is the plastic (polyethylene) impeller with a bearing/seal assembly linked to an external mixer drive.

The S.U.B. consists of the following components:

1. Outer Support Container—with a mixer drive complete with control unit and an electrical heater or water jacket.
2. Single-Use Bioreactor BPC—complete with agitator assembly, sparger, vent filter inlet and outlet ports, plus ports for integration of sensor probes and line sets. The S.U.B. BPC is supplied sterile and ready-to-use.
3. Drive Shaft—inserted into the S.U.B. BPC through the mixing drive motor and locked into the disposable agitator assembly.
4. Process Controls—temperature (not on water jacket) and agitation control are integrated into the S.U.B., but additional pH or dissolved oxygen (DO) controls must be supplied by the user.

The intended use of the Single-Use Bioreactor is as an animal cell culture bioreactor. The HyClone S.U.B. is not suitable for use as a microbial fermenter.

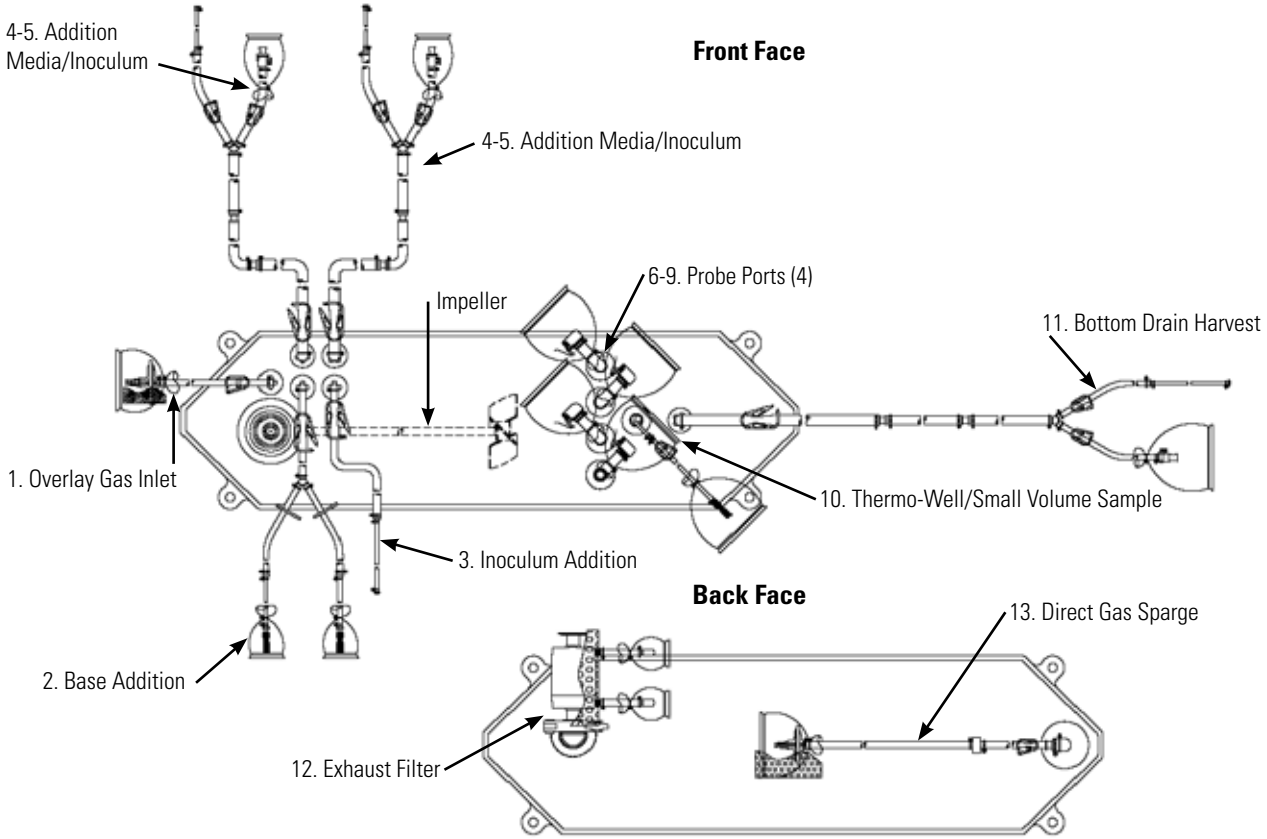
This document covers the 50, 100, 250, 500 and 1000 L original standard S.U.B. BPCs with disk sparge system. In addition to the change to the dual sparge system the new standard S.U.B. BPC line sets have been optimized to improve functionality. Details of the new standard S.U.B. BPCs along with full details of the other components of S.U.B. systems can be found in data sheets 026, 028, 029, 030 and 034. It is recommended that all customers transition to use the new dual sparge BPCs.

50 L Water Jacket S.U.B.

1000 L Water Jacket S.U.B.

Standard BPC Configurations – 50, 100 and 250 L

For use with tubing welder (CPC Quick Connect or Triclamp End Treatments)



Standard BPC Configurations

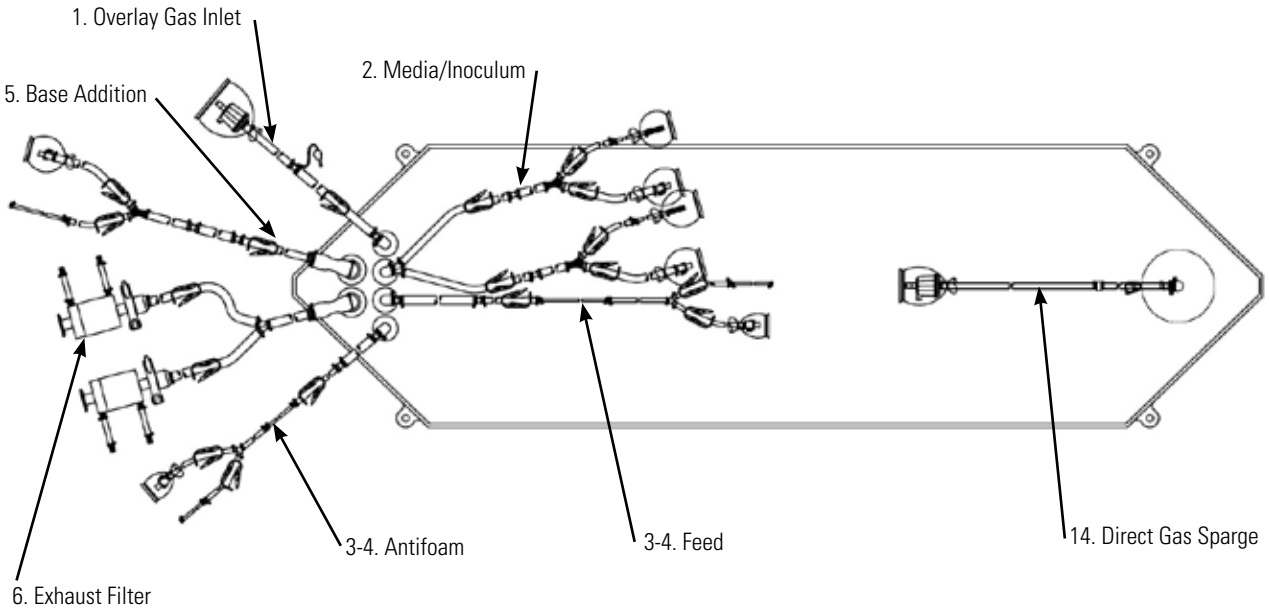
For use with tubing welder and CPC Quick Connects

Line	Description	Tubing Set (ID X OD X Length)	End Treatment	
			With Quick Connects	With Triclamps
1	Overlay Gas & Sparge	3/16" (4.8 mm) ID X 3/8" (9.5 mm) OD Silicone X 4" (10 cm)	Acro 50 Vent Filter	
2	Addition	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex® X 48" (122 cm) splits to 2 lines with: 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 36" (91 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm)	SmartSite® Valve Port	
3	Inoculum Addition	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 60" (152 cm) {for TC: 72" (183 cm)} reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm)	Plugged	SSV 3/4" mini TC
4-5	Media/Supplement Addition (2)	1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 48" (122 cm) reduced to 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 12" (30 cm) reduced to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 6" (15 cm) splits to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 3" (8 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm) and 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 12" (30 cm)	Plugged 1/4" MPC Body	Plugged SSV 3/4" mini TC
6-9	Connections for pH/ DO probes (4)	1/2" (12.7 mm) Tube ports	Pall® Kleenpak™ Aseptic Connector— KPCHT Series (Female)	
10	Thermo-Well/ Small Volume Sample	Thermo-Well Adapter for 1/4" (6.4 mm) Diameter. 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm)	SmartSite Valve Port	
11	Bottom Drain Harvest	1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 60" (152 cm) reduced to 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 12" (30 cm) reduced to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 6" (15 cm) splits to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 3" (8 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm) and 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 12" (30 cm)	Plugged 1/4" MPC Insert	Plugged 1 1/2" Molded TC
12	Exhaust Filter	1 1/2" (3.81 cm) Triclamp Port	0.2 Micron Exhaust Vent Filter	
13	Direct Gas Sparge	3/16" (4.8 mm) ID X 3/8" (9.5 mm) OD Silicone X 6" (15 cm) reduced to Check Valve and 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 48" (122 cm)	Acro 50 Vent Filter	

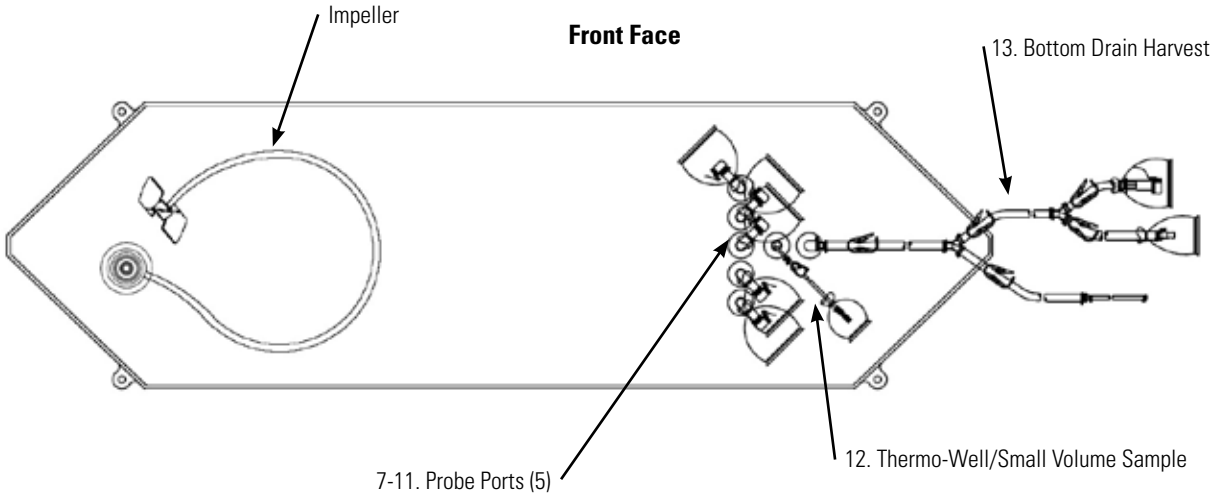
Standard BPC Configurations – 500 and 1000 L

For use with tubing welder, CPC Quick Connect (see Page 4 for line details)

Back Face



Front Face



Standard BPC Configurations

For use with tubing welder and CPC Quick Connects

Line	Description	Tubing Set (ID X OD X Length)	End Treatment
			With Quick Connects SH30748
1	Overlay Gas Inlet	3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 9" (23 cm) with inline disposable pressure transducer	Pall Kleenpak Gamma 0.2um
2	Media/Inoculum Addition	2 lines with: 1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 120" (305 cm) reduced to 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD PharMed® X 24" (61 cm) split to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 6" (15 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm) and 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 12" (30 cm)	SmartSite Valve Port, 3/8" MPC Body
3-4	Feed/Antifoam (2)	1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD Silicone X 3" (8 cm) reduced to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 4" (10 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 120" (305 cm) to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD PharMed X 24" (61 cm) splits to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 6" (15 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm) and 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 18" (46 cm) Dip Tube: 5" (10 cm) C-Flex	Plugged 1/4" MPC Body
5	Base Addition	3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 120" (305 cm) to 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD PharMed X 24" (61 cm) split to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 12" (30 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm) and 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 12" (30 cm) Dip Tube: 6" (15 cm) C-Flex	Plugged, 3/8" MPC Body
6	Exhaust Filter	7/8" (22.2 mm) ID X 1 1/8" (28.6 mm) OD Silicone X 3.5" (9cm) reduced to 1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 6" (15 cm) splits to 2 lines with: 1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 10" (25 cm) to 1 1/2" (3.81 cm) Triclamp Port	Pall Kleenpak Emflon® II 0.2 um
7-11	Connections for pH/ DO probes (5)	1/2" (12.7 mm) Tube ports	Pall Kleenpak Aseptic Connector (Female)
12	Thermo-Well/ Small Volume Sample	Thermo-Well Adapter for 1/4" (6.4 mm) Diameter 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 24" (61 cm)	SmartSite Valve Port
13	Bottom Drain Harvest	1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 60" (152 cm) split to 1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 6" (15 cm) split to 1/2" (12.7 mm) ID X 3/4" (19.1 mm) OD C-Flex X 24" (61 cm) and 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 24" (61 cm) and 3/8" (9.5 mm) ID X 5/8" (15.9 mm) OD C-Flex X 24" (61 cm) reduced to 1/8" (3.2 mm) ID X 1/4" (6.4 mm) OD C-Flex X 12" (30 cm)	Pall Kleenpak Aseptic Connector (Male), 3/8" MPC Insert, Plugged
14	Direct Gas Sparge	1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 6" (15 cm) to Check Valve to 1/4" (6.4 mm) ID X 7/16" (11.1 mm) OD C-Flex X 60" (152 cm)	Pall Kleenpak Gamma 0.2 um

Ordering Information for Standard BPC Products

Part Number	Description
SH30715.01	50 L S.U.B. bag with disk sparge and Quick Connect treatments
SH30725.01	50 L S.U.B. bag with disk sparge and Triclamp treatments
SH30744.01	100 L S.U.B. bag with disk sparge and Quick Connect treatments
SH30716.01	250 L S.U.B. bag with disk sparge and Quick Connect treatments
SH30726.01	250 L S.U.B. bag with disk sparge and Triclamp treatments
SH30748.01	500 L S.U.B. bag with disk sparge and Quick Connect treatments
SH30732.01	1000 L S.U.B. bag with disk sparge and Quick Connect treatments
SH30733.01	1000 L S.U.B. bag with disk sparge and Triclamp treatments

Presentation (as dry BPC systems):

Outer Packaging	Supplied 'flat-packed' Two polyethylene outer layers
Label	Description Product code Lot number Expiry date on outer packaging and shipping container
Sterilization	Irradiation (25 to 38 kGy) inside outer packaging
Shipping Container	Durable cardboard carton
Documentation	Certificate of Analysis provided with each lot for each delivery

Custom Options

Custom Hardware Options:

For stainless steel capabilities, please contact your sales representative for HyClone products for more information.

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3.8 Condenser System Data Sheet

Data Sheet 067 Rev 1

Thermo Scientific HyClone Single-Use Bioreactor (S.U.B.) Condenser System

The Thermo Scientific HyClone Single-Use Bioreactor (S.U.B.) Condenser System specifically supports the effective use of the HyClone 2000 L S.U.B. and is also available as an auxiliary product for all other S.U.B. systems. It efficiently condenses exhaust gases and transfers condensate back into the bioreactor, preventing potential vent filter blockage and reducing fluid loss due to evaporation. It is offered in both single and double chill-plate formats.

Overview:

The HyClone Condenser System protects against filter blockage by condensing out moister prior to exhaust gases reaching the vent filters. S.U.B. BioProcess Containers (BPCs) are not intended to operate under pressure, and fouled (blocked) exhaust filters lead to bag pressurization. While vent filter heaters may prevent condensate build-up in many instances, with larger bioreactors (e.g., 2000 L S.U.B.) this becomes less effective, whereas condensing out the moisture first is a more reliable method for preventing liquid from reaching the filters.

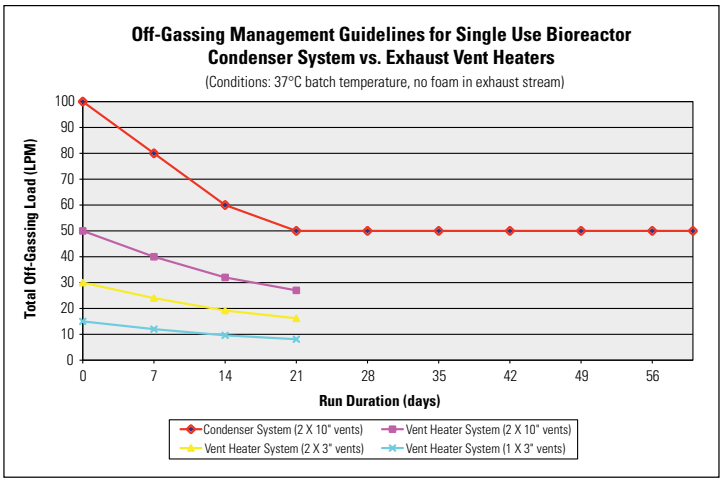
The S.U.B. Condenser System consists of the following components:

1. Cart and brackets—convenient means of organizing and transporting key working elements of the Condenser System.
2. Condenser (chill) plate—disposable double chamber condenser bag is secured to the condenser plate to cool exhaust gases. Up to two plates can be used per system.
3. Peristaltic pump—to return condensate to bioreactor.
4. Temperature control unit (TCU, also referred to as a chiller)—circulates water to cool the condenser plate.
5. Condenser disposables—the BPC (double-chambered bag), tubing, and exhaust filters though which the exhaust gases flow and are chilled, and in which the condensate collects and is returned to the bioreactor.

S.U.B. Condenser System

Item	Condenser System		
Power Options	115 VAC, 60 Hz or 230 VAC, 50 or 60 Hz		
Chiller Coolant	DI Water or Glycol (All validation testing was done with DI water)		
Total Dimensions	Length=37.88" (962 mm), Width=23" (584.2 mm), Height=75.13" (1908.2 mm)		
System Weight	293 lb (133 kg)		
Auto Restart Option	Available on pump and chiller. Recommended to be activated.		
Chiller Plate Cooling Surface Area	240 in^2 (1548 cm^2)		
Effective Bag Contact Surface Area on Chiller Plate	179 in^2 (1155 cm^2)		
Max Current Draw (115 VAC, 60 Hz)	11.4 A		
Item	**Condenser System Operating Information**		
	Min	**Recommended**	**Max**
Exhaust Gas Flow Capacity	0 lpm	≤50 lpm @ 0.1 psi	100 lpm w/ 5° C Chiller 95 lpm w/ 8° C Chiller 75 lpm w/ 10° C Chiller
Chiller Set Point	5°C	5°C	10°C
Peristaltic Pump Speed Set Point	12 rpm	12 rpm	30 rpm
Chiller Internal Pressure Regulator (IPR) Set Point	7 psi	≤14.7 psi	30 psi

Table 1. Condenser System Operating Parameters



Graph 1. Condenster vs. Exhaust Vent Filter Heaters

Performance Guidelines and Comparison

Choosing the best exhaust vent configuration for the S.U.B. is application specific. For most S.U.B. configurations it will depend upon a combination of many variables (e. g., exhaust flow rate, process stability, reliability expectations, culture run duration or concern for evaporation loss). The accompanying graph provides a simple process-based reference for determining if a vent heater option will be sufficient or if a Condenser System is preferred. Typically, any off-gassing flow rates approaching 50 lpm or culture durations exceeding 10 days should consider utilizing the Condenser System.

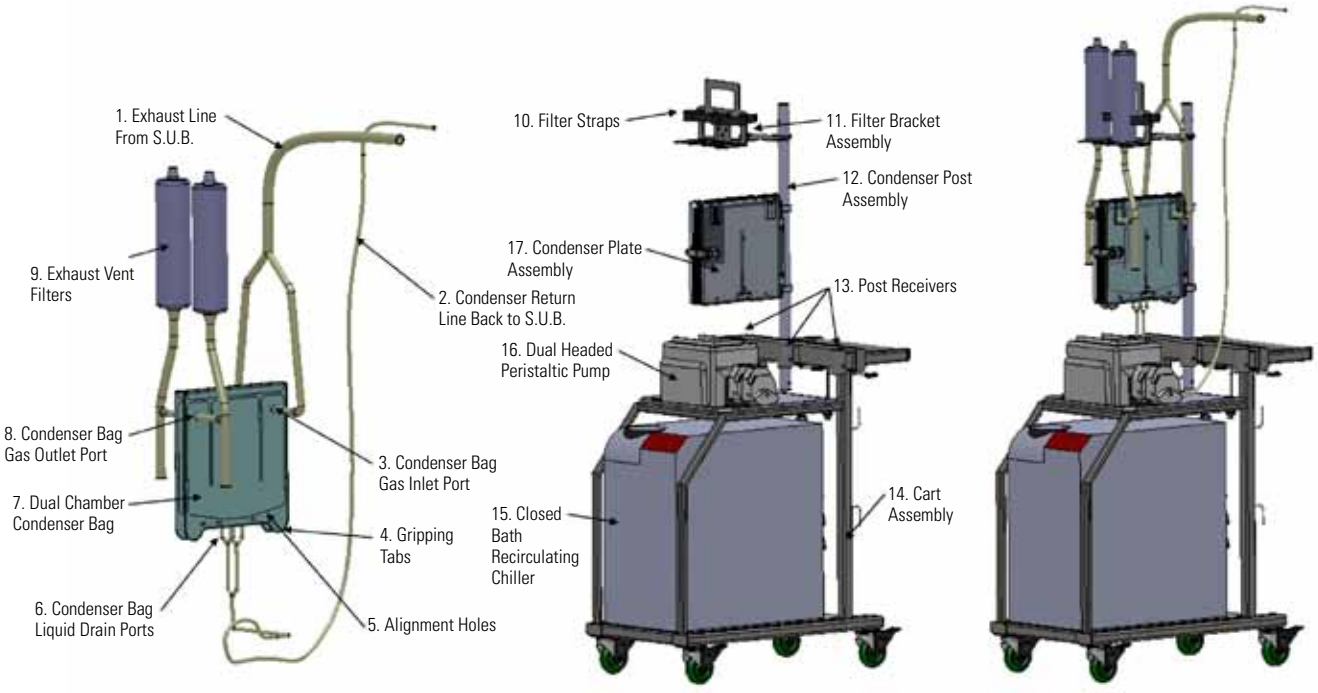
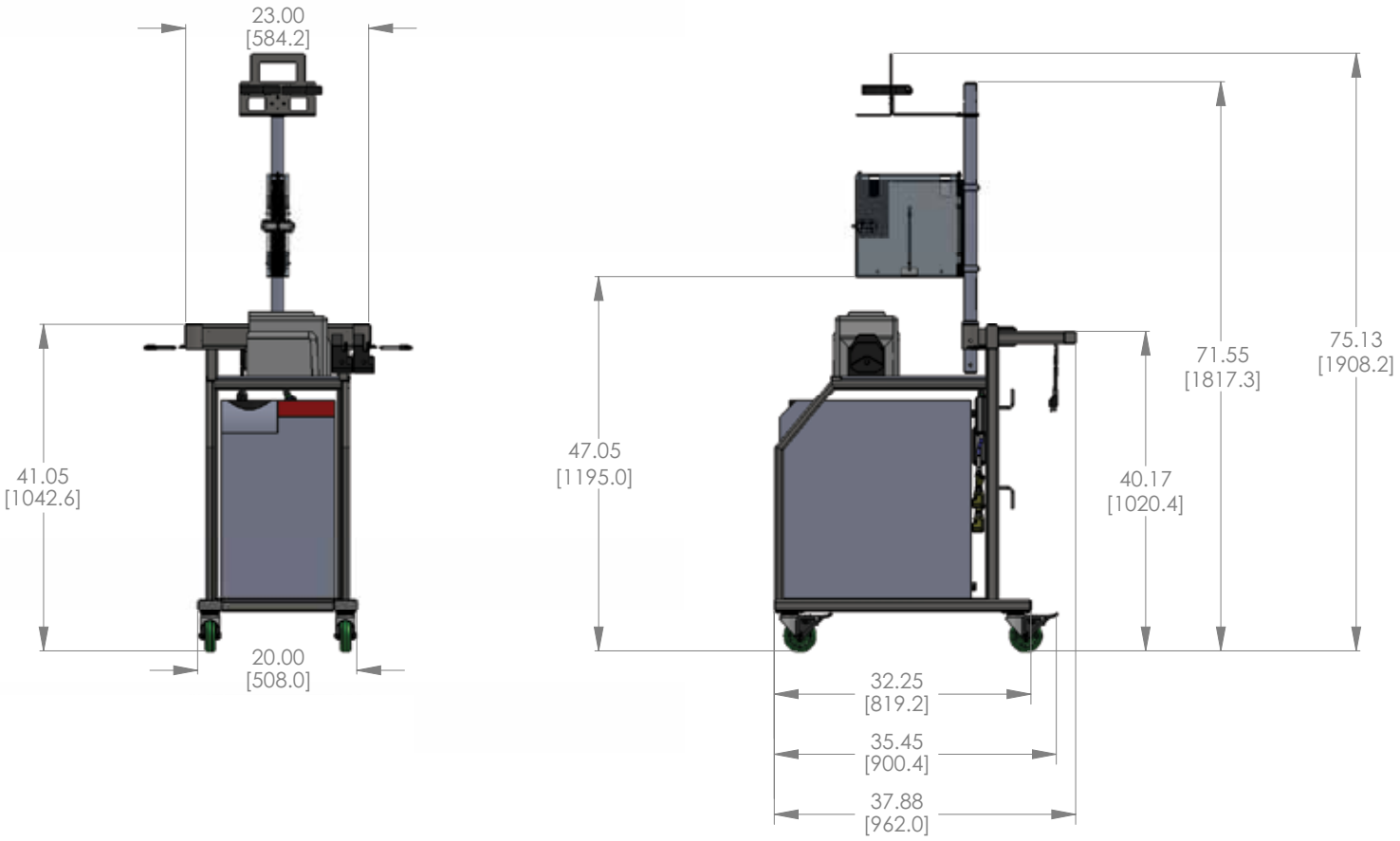


Figure 1. Condenser System Overview

Item	Description
1	Exhaust Line From S.U.B. – to vent S.U.B. BPC, maintaining a non-pressurized system
2	Condenser Return Line Back to S.U.B. – to transfer condensate into bioreactor
3	Condenser Bag Gas Inlet Port – receives S.U.B. exhaust for cooling
4	Gripping Tabs – enable operator to securely position condenser bag
5	Alignment Holes – match up with condenser plate posts to maintain bag position
6	Condenser Bag Liquid Drain Ports – condensate flows through these ports to bioreactor
7	Dual Chamber Condenser Bag – gas circulates through integral channels for chilling
8	Condenser Bag Gas Outlet Port – "dry" exhaust gases exit condenser bag toward exhaust filters
9	Exhaust Vent Filters – vent exhaust gases to ambient atmosphere
10	Filter Straps – for securing vent filters in position
11	Filter Bracket Assembly – support vent filters
12	Condenser Post Assembly – supports condenser plate and filter brackets
13	Post Receivers – three alternative for post position or additional posts
14	Cart Assembly – for organizing and transporting key working elements of the condenser system
15	Closed Bath Recirculating Chiller (TCU) – circulates chilled water for cooling condenser plate
16	Dual Headed Peristaltic Pump – to return condensate to bioreactor
17	Condenser Plate Assembly – holds condenser bag for chilling exhaust gases

Table 2. Condenser System Overview

Part Number	Description
SV50232.01	Complete Condenser System (120 V) including cart, chill plate and mounting post with filter brackets, TCU, and pump
SV50232.02	Complete Condenser System (240 V) including cart, chill plate and mounting post with filter brackets, TCU, and pump
SV50232.21	Condenser assembly including chill plate and mounting post with filter brackets (Option: Allowing two chill plates per systems)
SV50232.23	Thermoflex 900 TCU (115 VAC/60 Hz) with necessary plumbing
SV50232.24	Thermoflex 900 TCU (240 VAC/50 or 60 Hz) with necessary plumbing
SV50241.01	Thermo Scientific Masterflex Pump (115 VAC/50 or 60 Hz or 230 VAC/50 or 60 Hz)



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3.9 Load Cells Kit Data Sheet

Load Cell kits are available for the Thermo Scientific HyClone Single-Use Bioreactor (S.U.B.) and Single-Use Mixer (S.U.M.). Kits can be configured for new or existing units.

Data Sheet 048 Rev 2

Thermo Scientific HyClone Load Cell Kits

Overview:

The FLEXMOUNT® Weigh Modules are used to enable weight measurements. They operate as a mechanical suspension system on the Thermo Scientific HyClone Single-Use Bioreactor (S.U.B.) and the Thermo Scientific HyClone Single-Use Mixer (S.U.M.).

Load Cell systems include three cells, summing block, display and wiring. They can be purchased either at the time of equipment sale or as retro-fit kits for existing S.U.B. and S.U.M. units. Units can be load cell equipped as an option for the 50-500 L S.U.B. and the 50-2000 L S.U.M. units. Load cells come standard on the 1000 L S.U.B.

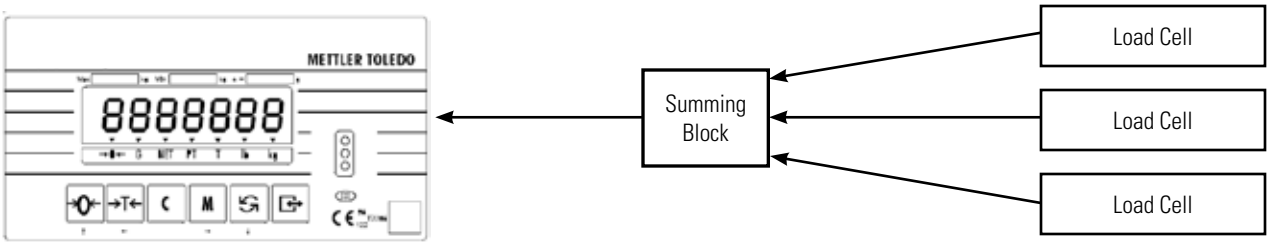
FLEXMOUNT Load Cell

Load Cell Specifications:

Weigh Module Parameter		Unit of Measure	Specification			
			50 & 100 L S.U.B. 50 L S.U.M	250 L S.U.B. 200 L S.U.M.	500 & 1000 L S.U.B. 500 & 1000 L S.U.M	2000 L S.U.M
Model Number			0958 FLEXMOUNT			
Rated Capacity		kg (lb)	113 (250)	220 (500)	550 (1250)	1100 (2500)
Load Limit, Safe	Stainless Steel	kN (lb)	1.7 (375)	3.3 (750)	8.3 (1875)	16.6 (3750)
Maximum Horizontal Force	Transverse[1]	kN (lb)	1.1 (250)	2.2 (500)	4.1 (920)	8.2 (1840)
	Longitudinal[2]	kN (lb)	1.1 (250)	2.2 (500)	5.6 (1250)	11.2 (2500)
Maximum Top Plate Travel	Transverse	± mm (in)	3.01 (0.12)			
	Longitudinal	± mm (in)	3.01 (0.12)			
Maximum Uplift Force		kN (lb)	22.2 (5000)			
Weight (including load cell), nominal		kg (lb)	7 (15.5)			
Material			304 Stainless Steel			

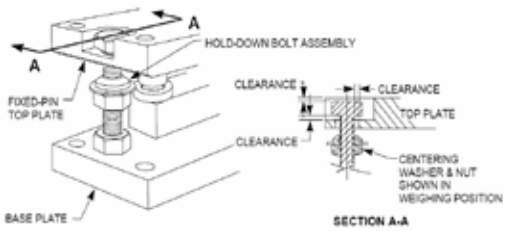
[1] Maximum horizontal force that can be applied to the top plate in a direction transverse to the longitudinal axis of the load cell. Applies to fixed-pin module and semi-float module assembled in standard (radial mounting) position.
[2] Maximum horizontal force that can be applied to the top plate in a direction parallel to the longitudinal axis of the load cell. Applies to fixed-pin module and semi-float module assembled in nonstandard (tangential mounting) position.

Load Cell System:



Mettler Toledo Panel Mount Display standard with 1000 L S.U.B. only.

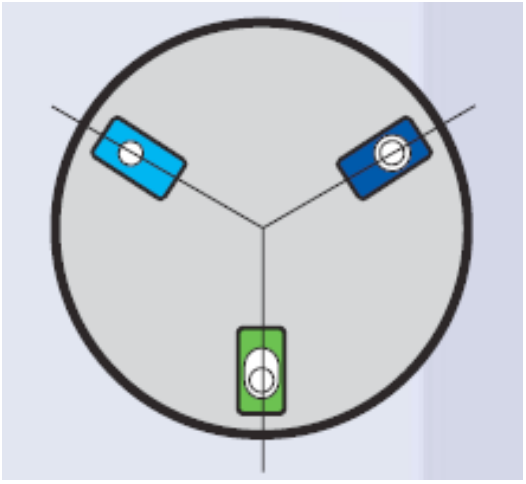
Mettler Toledo Cart or Wall mount option for 50-500 L S.U.B. and 50-2000 L S.U.M.



Unlocking Load Cell

Load Cell Mounting:

Radial Mounting:



Load Cells are typically radial mounted. Locations for mounting are altered on some units to allow easy access to bottom drain or sparge mechanisms and tubing.

Technical Information:

For more information on load cells, calibration methods, Mettler Toledo terms or service please go to the Mettler-Toledo Web site: http://us.mt.com or your local representative.
For information on manuals please refer to the following documents on the Mettler Toledo Web site.

F15175600A—Manual for Load Cells
16528600A—Manual for Panther Display

Ordering Information for Single-Use Bioreactor and Single-Use Mixer:

Load Cells:

Volume	Retro Fit Kit To Be Assembled By Customer	Load Cells To Be Assembled By Manufacturer	Description Of Panel Communication Platform
50 & 100 L	SV50194.01	SV50194.11	Panel Mount display, Modbus® Plus Interface
200 & 250 L	SV50193.01	SV50193.11	
500 & 1000 L	SV50218.01	SV50218.11	
2000 L	SV50227.01	SV50227.11	
50 & 100 L	SV50194.02	SV50194.12	Panel Mount display, Allen-Bradley® Rio Interface
200 & 250 L	SV50193.02	SV50193.12	
500 & 1000 L	SV50218.02	SV50218.12	
2000 L	SV50227.02	SV50227.12	
50 & 100 L	SV50194.03	SV50194.13	Panel Mount display, Analog Output Interface
200 & 250 L	SV50193.03	SV50193.13	
500 & 1000 L	SV50218.03	SV50218.13	
2000 L	SV50227.03	SV50227.13	
50 & 100 L	SV50194.04	SV50194.14	Panel Mount display, Profibus™ Interface
200 & 250 L	SV50193.04	SV50193.14	
500 & 1000 L	SV50218.04	SV50218.14	
2000 L	SV50227.04	SV50227.14	
50 & 100 L	SV50194.05	SV50194.15	Wall Mount display, Modbus® Plus Interface
200 & 250 L	SV50193.05	SV50193.15	
500 & 1000 L	SV50218.05	SV50218.15	
2000 L	SV50227.05	SV50227.15	
50 & 100 L	SV50194.06	SV50194.16	Wall Mount display, Allen-Bradley® Rio Interface
200 & 250 L	SV50193.06	SV50193.16	
500 & 1000 L	SV50218.06	SV50218.16	
2000 L	SV50227.06	SV50227.16	
50 & 100 L	SV50194.07	SV50194.17	Wall Mount display, Analog Output Interface
200 & 250 L	SV50193.07	SV50193.17	
500 & 1000 L	SV50218.07	SV50218.17	
2000 L	SV50227.07	SV50227.17	
50 & 100 L	SV50194.08	SV50194.18	Wall Mount display, Profibus™ Interface
200 & 250 L	SV50193.08	SV50193.18	
500 & 1000 L	SV50218.08	SV50218.18	
2000 L	SV50227.08	SV50227.18	
50 & 100 L	SV50194.09	SV50194.19	No Display Orderded
200 & 250 L	SV50193.09	SV50193.19	
500 & 1000 L	SV50218.09	SV50218.19	
2000 L	SV50227.09	SV50227.19	
50 & 100 L	SV50194.30	SV50194.20	Panel Mount display, Device Net™ Interface
200 & 250 L	SV50193.30	SV50193.20	
500 & 1000 L	SV50218.30	SV50218.20	
2000 L	SV50227.30	SV50227.20	
50 & 100 L	SV50194.31	SV50194.21	Wall Mount display, Device Net™ Interface
200 & 250 L	SV50193.31	SV50193.21	
500 & 1000 L	SV50218.31	SV50218.21	
2000 L	SV50227.31	SV50227.21	

Data Sheet

The 1000 and 2000 L S.U.B.s come standard with load cells. The tables below list the S.U.B. part numbers and their corresponding load cell communications platforms.

1000 L S.U.B. Systems

S.U.B Specification Numbers	Volume	Description of Panel Communication Platform
Electric Resistive Heater		
SV50174.01	1000 L	Modbus Plus Interface
SV50174.02	1000 L	Allen-Bradley RIO Interface
SV50174.03	1000 L	Analog Output Interface
SV50174.04	1000 L	Profibus Interface
SV50174.05	1000 L	Device Net Interface
Water Jacket Heater		
SV50174.11	1000 L	Modbus Plus Interface
SV50174.12	1000 L	Allen-Bradley RIO Interface
SV50174.13	1000 L	Analog Output Interface
SV50174.14	1000 L	Profibus Interface
SV50174.15	1000 L	Device Net Interface


1000 L S.U.B.

2000 L S.U.B. Systems

S.U.B Specification Numbers	Volume	Description of Panel Communication Platform
Water Jacket Heater		
SV50223.11	2000 L	Modbus Plus Load Cell Interface
SV50223.12	2000 L	Allen-Bradley Load Cell Interface
SV50223.13	2000 L	Analog Output Load Cell Interface
SV50223.14	2000 L	Profibus Load Cell Interface
SV50223.15	2000 L	DeviceNet Load Cell Interface


2000 L S.U.B.

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3.10 S.U.B. Vent Filter Heater Data Sheet

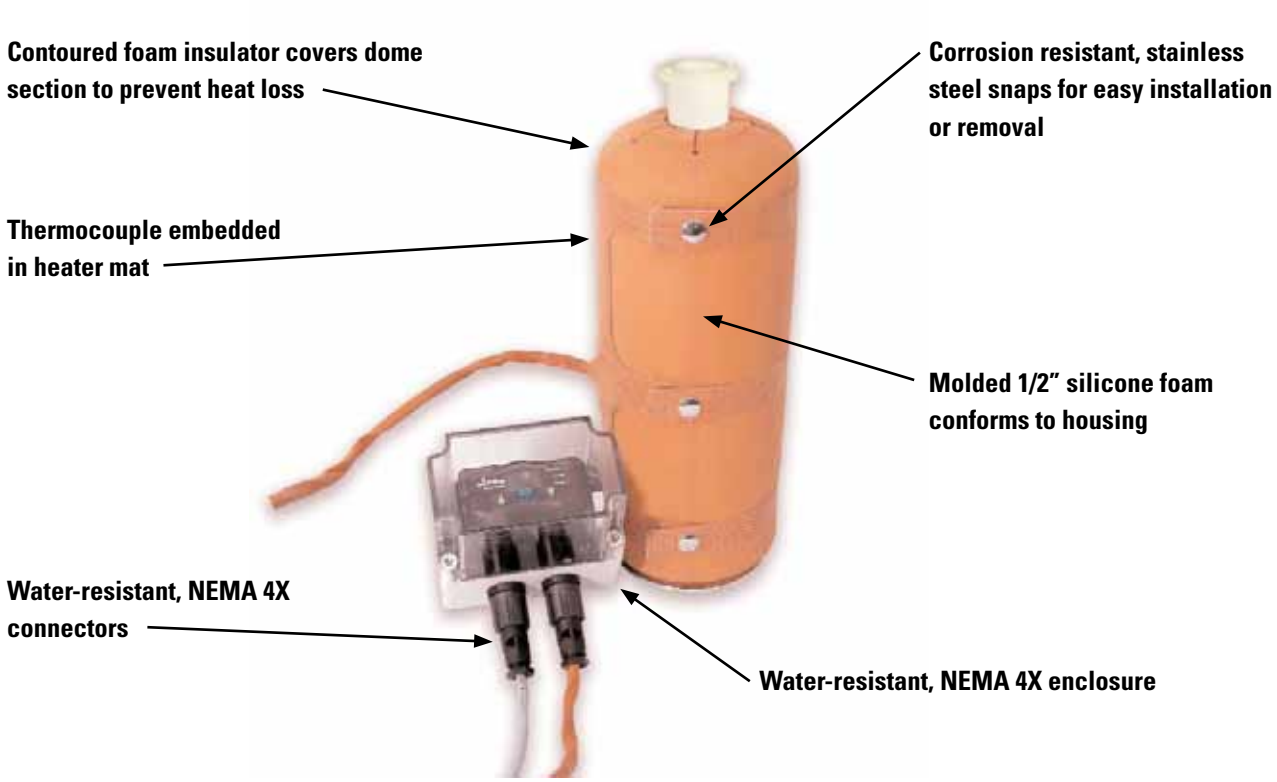
A vent filter heater system is an additional option for the Thermo Scientific HyClone Single-Use Bioreactor (S.U.B.) system. It is supplied as an accessory for those customers who require it to protect the vent filter on the standard S.U.B. BioProcess Container (BPC).

Thermo Scientific HyClone Single-Use Bioreactor Vent Filter Heater

Overview:

The resistive heating element is fully insulated with molded silicone foam and is easily secured around the filter by use of snap retainers. This custom molded heater creates a perfect fit that will fully encapsulate the exhaust filters for consistent temperature regulation. The temperature controller is preset specifically for the HyClone Single-Use Bioreactor (S.U.B.) at 50°C and has an adjustable temperature range of 0-220°C. Temperatures above 60°C are not recommended for the filters used on the S.U.B. The controller has programmable logic and is equipped with a low temperature alarm output. Water protection is recommended for vent heater installation that may encounter wet conditions while in use. Choose a power cord with a GFCI, or for the utmost protection a water resistant (NEMA) version of the 48 series controller can be ordered as part of a complete kit. The vent filter heater system stands alone and does not integrate with the control system of the S.U.B. controller. The system consists of the following components: Heater, Controller and Power Cord. Refer to the vent filter heater user's manual included in the S.U.B. ETP for further information.

System Components and use:



Ordering Instructions

Standard 48 series vent filter heaters for use with Pall KA3 vent filters:

Selecting a complete kit will require two part numbers, a vent filter heater/controller (SV50191.01 for 115 VAC or SV50191.02 for 230 VAC) and the suitable power cord for your installation (SV50191.02, or .04 through .08). **NOTE:** SV50191.10 does not have a controller and is for custom installations only.

Part Number	Description	Additional Information
SV50191.01	Vent Filter Heater with Programmable Controller (100-120 VAC)	Includes low temp alarm. Preset temp 50°C
SV50191.02	Power Cord (100-120 VAC)	For use in U.S./Japan, NEMA 5-15P with 12' leads
SV50191.03	Vent Filter Heater with Programmable Controller (200-240 VAC)	Includes low temp alarm. Preset temp 50°C
SV50191.04	Power Cord (240 VAC)	For use in United Kingdom, BS1363 with 10' leads
SV50191.05	Power Cord (240 VAC)	For use in Europe, CEE7/7 with 12' leads
SV50191.06	Power Cord (100-120 VAC)	For use in U.S./Japan, NEMA 5-15P with 12' leads and GFCI
SV50191.07	Power Cord (240 VAC)	For use in United Kingdom, BS1363 with 12' leads and GFCI
SV50191.08	Power Cord (240 VAC)	For use in Europe, CEE 7/7 with 12' leads and GFCI
SV50191.09	Extension Cord for Series 48 Heater (100-240 VAC)	For use between heater and controller, 10'
SV50191.10	Vent Filter Heater with RTD (two wire Pt-100), (100-120 VAC/17-24 W)	Includes sheathed 20' pig-tail lead

NEMA rated 48 series vent filter heater kits for use with Pall KA3 vent filters:

Sold as a kit which includes vent filter heater, controller with a water-tight enclosure, quick connects, and installation power cord.

Part Number	Description	Additional Information
SV50191.11	NEMA rated Vent Heater w/ Programmable Controller (100-120VAC), power cord	Includes low temp alarm, preset temp 50°C, power cord w/ flying leads
SV50191.13	NEMA rated Vent Heater w/ Programmable Controller (200-240VAC), power cord	Includes low temp alarm, preset temp 50°C, power cord w/ flying leads

NEMA rated 48 series vent filter heater kits for use with Meissner Ultracap 10" vent filters:

Sold as a kit which includes vent filter heater, controller with a water-tight enclosure, quick connects, and installation power cord.

Part Number	Description	Additional Information
SV50191.16	NEMA rated Vent Heater w/ Programmable Controller (100-120VAC)	Includes low temp alarm, preset temp 50°C , 20' NEMA 5-15 power cord for U.S./Japan
SV50191.17	NEMA rated Vent Heater w/ Programmable Controller (200-240VAC)	Includes low temp alarm, preset temp 50°C, 20' BS1363 power cord for United Kingdom
SV50191.18	NEMA rated Vent Heater w/ Programmable Controller (200-240VAC)	Includes low temp alarm, preset temp 50°C, 20' CEE7/7 power cord for Europe
SV50191.19	NEMA rated Vent Heater w/ Programmable Controller (200-240VAC)	Includes low temp alarm. Preset temp 50°C, 12' IEC320 power cord for 2000 L SUB control box

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Section 4 Troubleshooting

Symptom Single-Use Bioreactor will not operate.

Remedy Check power supply.

- Verify main electrical plug connection at wall outlet, verify position of main power disconnect, and verify position of Emergency Stop switch.
- Verify condition of main electrical circuit breaker of facility. If protection breaker has been tripped, determine fault condition. The condition may exist where other electrical systems are requiring current loads beyond those allowed by the breaker. S.U.B. system should be placed on its own electrical circuit.
- Disconnect main power cord. Inspect electrical circuit breakers and fuses inside the electrical enclosure of the S.U.B. controller. Determine fault condition by visual inspection. If fault condition can not be determined by visual inspection, contact manufacturer.

Symptom Single-Use Bioreactor temperature is below target or slow to respond.

Remedy Check temperature controller and sensor.

- Verify the temperature probe (RTD) is not loose and has been fully inserted into the S.U.B. BPC thermo-well.
- Verify thermo-well has been filled with sufficient glycerol to aid in heat transfer.
- Verify that temperature controller is enabled. Indicator light (green LED labeled–C1) will illuminate when temperature controller is cycling heater to maintain target temperature.
- Verify mixer is operating, safety interlock will not allow heaters to warm without the mixer in operation.
- Verify system is filled with sufficient volume of fluid. There must be enough volume of media (minimum volume) in S.U.B. BPC to provide contact with the bag (add more media if BPC is not touching heater area).

Symptom Mixer controller does not respond to user inputs.

Remedy Allow speed to stabilize before using key-pad interface.

- Rapidly adjusting speed control in an excessive manner may require several seconds for speed stabilization.
- Wait ten seconds and then attempt to adjust speed at key-pad interface.

- Users should verify the position of the input select switch of the VFD. If the toggle switch is not in the middle position, the controller will not be able to receive control inputs from the control keypad on the front panel.

Symptom Dissolved Oxygen (DO) readings are low or slow to respond.

Remedy Check physical condition of the DO probe, calibration of the DO probe, flow rate of gas into S.U.B.

- DO probes require routine maintenance; replace damaged probe or membrane.
- Verify DO probe calibration relative to set-points of zero and span.
- Inspect line sets connected to direct sparges for restriction (closed tubing clamp, pinched line, low supply pressure).

Symptom Direct membrane sparge does not seem to be working although gas is present.

Remedy Allow sparge membrane to purge.

- If the S.U.B. is filled with liquid and allowed to sit idle for extended periods of time without gas being supplied to the sparge, liquid can accumulate between the membrane and check valve. Various media additives may restrict the membrane temporarily. Several minutes of gas pressure being supplied to the sparge should purge the membrane, allowing it to function properly.
- Certain operating conditions can create situations when the sparge membrane may become restricted due to insufficient line pressure from the bioreactor controller gas feed line. Increasing the flow rate to 1 liter per minute, or momentarily raising the pressure regulator outlet pressure to 5 psi (0.34 bar) may alleviate the problem. Alternatively, several seconds at this higher pressure will allow the membrane to purge pores that may be blocked due to the presence of accumulated liquid.

Symptom DO readings are erratic or unstable.

Remedy Adjust bioreactor controller to suite the volume of the S.U.B. system.

- Many different parameters can effect the ability of a bioreactor controller to effectively maintain a target setpoint during process control. Modern controllers utilize computer algorithms to adjust targeted parameters, the most common technique is that of tunable controller that uses variables of PID. Tuning these PID values to the specific characteristics of the system dynamics will in most cases stabilize process parameters to an acceptable level. It is recommended that S.U.B. users consult the user manual of the particular bioreactor controller being used.
- A grounding reference to the media can be created by using a grounding lead between the tank and the body of the stainless steel DO probe or to the stainless steel connector (if present) on the sample line of the S.U.B BPC.

Symptom Most traditional systems utilize a condenser or exhaust vent heater to help manage condensate; is this necessary for the S.U.B.?

Remedy Extensive testing has found that an exhaust heater or a condenser is not typically required under normal operating conditions for S.U.B.s 500 L or smaller. However more demanding applications may warrant an exhaust vent heater which is available from your sales rep.

Symptom I typically use level sensors to control volume and feed rate or supplement during a bioreactor run; how would I do this with the S.U.B.?

Remedy Use load cells or a scale to control volumes based upon weight.

- The S.U.B. is not equipped with level sensors. However, the S.U.B. can be setup to allow supplement feeds and volumes to be managed by weight. Please refer to Section 3 for skid dimensions for sizing of scales.

Symptom pH levels are questionable or out of range.

Remedy Verify calibration of probe, utilize either media or gas buffers.

- pH levels can be managed in a similar manner to conventional bioreactors once calibration of the probe is verified by use of an off-line sample. Carbon dioxide gas sparged through the media or headspace, biocarbonate levels in the media, and the addition of liquid titrant solutions all serve to manage the pH balance of the bioreactor environment. See Section 2.5 - Probe Assembly instructions for more information on probe calibration.
- A grounding reference to the media can be created by using a grounding lead between the tank and the body of the stainless steel DO probe or to the stainless steel connector (if present) on the sample line of the S.U.B BPC.

Symptom S.U.B. BPC seems overly tight or overpressure.

Remedy Verify bag is venting and inspect for cause of overpressure.

- Reduce inlet gas flow rate of overlay and direct sparge.
- Inspect exhaust filter for restriction or blockage.
- Excessive foaming should be avoided for several reasons. If foam levels are allowed to reach the exhaust filter, the filter will become restricted resulting in excessive internal pressure within the confines of the S.U.B. This may cause product failure and impending burst of the S.U.B. BPC.

Symptom Noise emitted from the BPC mixer assembly.

Remedy No action required.

- The bearing port assembly supplied with the S.U.B. is an important component in maintaining a sterile environment during cell growth. The special seals used in the S.U.B. may generate some noise during operation, particularly after the first day of operation. This noise may vary in intensity and frequency but generally has no significant effect upon performance or overall durability of the S.U.B. BPC during the intended life of the product.

Symptom We forgot to introduce the pH and DO probes prior to media fill; can we still make a sterile connection under these conditions?

Remedy Yes, as long as the clamps were closed on the Kleenpak Connector probe ports before liquid fill.

- The Kleenpak connectors must be dry to make the connection of the probe assemblies. When media is already present in the S.U.B., follow the probe insertion procedures as outlined in Section 2.5: Probe Assembly. Some fluid may enter the bellows when the probe is inserted into a BPC already filled with media.

Symptom I am not familiar with the use of the Pall Kleenpak Connectors and am concerned about making connections. What can I do to ensure a successful connection using this system?

Remedy Familiarize yourself with the Pall Kleenpak Connector instructions found in Section 2.7 before beginning.

- When a connection is being made, visually evaluate the status of the four locking external clips and verify they are tightly secured (the snap should be audible for all four clips when pressing the connectors together). Always make sure the four locking clips are fully engaged for the male/female connection before removing the paper strips.
- A common cause for a leaky Kleenpak is an error in the final step of seating the tapered barrels of the male/female connector. There are a series of concentric rings inside the male connector (0.3” in front of the black O-ring) Visually verify that the four internal clips are on the last set of rings. Using both hands place connector flanges between index fingers and thumbs and squeeze until properly seated.

Symptom

We are not achieving the cell growth we expected in the S.U.B. while running under our normal bioreactor agitation and sparging rates. What should we do?

Remedy

Reduce agitation and sparging rates.

- Often low cell viability and cell growth can be attributed to excessive sparging or agitation. It is recommended that users reduce their sparge rate compared to what they might use in a conventional bioreactor. Gas flow rates supplied as overlay should also be reduced as much as possible. Too much gas creates excess foam and higher shear conditions. Provide only the level of agitation needed: low viability and lysed cells, reduce agitation speed—cell aggregation and settling, increase agitation. Media formulation can also have a large affect on cell culture growth in the S.U.B. Surfactants such as Pluronic decrease shear and increase k_La, but at a cost of increased foaming. Thermo Scientific can offer custom media especially for the S.U.B. and customer's specific cell line(s).

Symptom

Excessive foam in the bioreactor headspace.

Remedy

Alter the liquid surface tension related to the culture media and/or sparge gas.

- A media supplement of antifoam can be used in the S.U.B. These serve to lower the surface tension of the media and will reduce the presence of foam.
- High sparge rates of air can result in the presence of excessive foam. Testing has shown that sparging with oxygen will typically result in dramatic reduction of foam in the headspace.

Section 5 Ordering Information

This section covers the following information:

5.1 Ordering Information

Disposables

Standard BPC Products

Part Number	Description	Additional Information
SH30774.01	50 L S.U.B. BPC	Standard dual sparge bags featuring an open pipe sparge and a porous frit sparge. All S.U.B. BPCs provided gamma-sterilized.
SH30774.02	100 L S.U.B. BPC	
SH30774.03	250 L S.U.B. BPC	
SH30774.04	500 L S.U.B. BPC	
SH30774.05	1000 L S.U.B. BPC	
SH30774.07	2000 L S.U.B. BPC	
SH30774.08	2000 L S.U.B. BPC w/o condenser assembly	

Custom BPC Products

Category	Options/Capability	Remarks
Tubing Type	C Flex, platinum cured silicone, PVC, Pharmed®, PharmaPure®	More information in selection guide of BPC catalog
Tubing Size	Specific lengths of 1/8" ID to 1" ID	ID limitations due to port size
Connectors	Luers, CPC Quick Connects, SIP connectors, Triclamp, Kleenpak, Lynx®, SmartSite®, Clave®, Lynx steam thru, CPC Steam Thru, Gore steam valve, Gore Mini TC, BioQuate (GE), PAW SterilEnz®, end plug, etc.	Refer to selection guide in BPC catalog for further information by connection type. **Note:** Only option for probe port connections is Kleenpak.
Kleenpak (i.e., probe) ports	Additional ports: second row of 4 for 50 L to 250 L S.U.Bs.; second row of 5 for 500 L and 1000 L S.U.B.s	
Disposable sensors	Pressure sensor: Pendotech for 50 L to 250 L S.U.B. (comes standard on 500 L and 1000 L) DO – Finesse DO and pH – PreSens Availability of various other disposable sensors currently pending.	
Addition of ports/lines (other than 2nd row of probe ports)	Limited engineer-to-order customization possible such as additional media lines and vent filter lines. Requires economic justification.	Dependent on location in bag and compatibility with hardware
Port sizes	Limited customization possible as engineer-to-order with justification.	Dependent on location in bag and fit with hardware (e.g., 1" ID port on harvest line)
Re-arrangement of lines on existing ports	Limited customization possible, e.g., moving sample/tempwell port to a probe tube port, or swapping overlay inlet line with supplement line.	Dependent on location in bag and fit with hardware
Sparger	Dual sparger (open pipe plus porous frit) standard. Can do an engineer-to-order for one or the other alone. Make-to-order bags will be built around standard dual sparger chamber.	
Dip tube lines	Limited customization possible. Suggested use through 1" port, so this is engineer-to-order. Otherwise must use ferrule approach.	Length cannot interfere with impeller and shaft. Typical is 10" or shorter.
Overlay and Sparge Line Filters	Can use disposable (capsule) filter other than standard hydrophobic vent filter with Emflon II.	
Vent Filters	Standard is Pall Kleenpak 0.2 micron exhaust vent filter.	**NOTE:** Vent filter heater configuration restricts options
Vent Filter Tubing Length	Extended filter height above the S.U.B. bag is make-to-order.	Must be compatible with a vent filter bracket option
Filters on Media and Supplement Inlets	Choice of filters for inlets used to sterile filter incoming media or supplements.	

5.2 Ordering Information

Hardware

Standard S.U.B. Products

50 L, 100 L, 250 L and 500 L S.U.B. Systems Include: 304 stainless steel outer support container with swivel caster platform, variable speed agitation controller, motor, drive assembly with shaft, PID temperature controller (resistive only), RTD sensor, integrated resistive heating element or jacket, probe shelf and standard tool set.

Part Number	Description
SV50171.01	50 L S.U.B., Electric Resistive Heater, US version (120 VAC)
SV50171.02	50 L S.U.B., Electric Resistive Heater, EU version (240 VAC)
SV50171.03	50 L S.U.B., Water Jacket, US version (120 VAC)
SV50171.04	50 L S.U.B., Water Jacket, EU version (240 VAC)

Part Number	Description
SV50197.01	100 L S.U.B., Electric Resistive Heater, US version (120 VAC)
SV50197.02	100 L S.U.B., Electric Resistive Heater, EU version (240 VAC)
SV50197.03	100 L S.U.B., Water Jacket, US version (120 VAC)
SV50197.04	100 L S.U.B., Water Jacket, EU version (240 VAC)

Part Number	Description
SV50172.01	250 L S.U.B., Electric Resistive Heater, US version (120 VAC)
SV50172.02	250 L S.U.B., Electric Resistive Heater, EU version (240 VAC)
SV50172.03	250 L S.U.B., Water Jacket, US version (120 VAC)
SV50172.04	250 L S.U.B., Water Jacket, EU version (240 VAC)

Part Number	Description
SV50200.02	500 L S.U.B., Electric Resistive Heater, US/EU version (208/240 VAC)
SV50200.04	500 L S.U.B., Water Jacket, US/EU version (208/240 VAC)

1000 L S.U.B. Systems Include: 304 stainless steel outer support container with swivel caster platform, variable speed agitation controller, motor, drive assembly with shaft, PID temperature controller, three load cells with summing block, display and wiring, RTD sensor, integrated resistive heating element, probe shelf, and standard tool set.

Part Number	Description
SV50174.01	1000 L S.U.B. Electric Resistive Heater, Modbus Plus Interface (240 VAC)
SV50174.02	1000 L S.U.B. Electric Resistive Heater, Allen-Bradley Interface (240 VAC)
SV50174.03	1000 L S.U.B. Electric Resistive Heater, Analog Output Interface (240 VAC)
SV50174.04	1000 L S.U.B. Electric Resistive Heater, Profibus Interface (240 VAC)
SV50174.05	1000 L S.U.B. Resistive Heater, DeviceNet Interface (240 VAC)

Part Number	Description
SV50174.11	1000 L S.U.B. Water Jacket, Modbus Plus Interface (240 VAC)
SV50174.12	1000 L S.U.B. Water Jacket, Allen-Bradley Interface (240 VAC)
SV50174.13	1000 L S.U.B. Water Jacket, Analog Output Interface (240 VAC)
SV50174.14	1000 L S.U.B. Water Jacket, Profibus Interface (240 VAC)
SV50174.15	1000 L S.U.B. Water Jacket, DeviceNet Interface (240 VAC)

2000 L S.U.B. Systems Include: 304 stainless steel outer support container, variable speed agitation controller, motor, drive assembly with four segment drive shaft, RTD sensor, integrated water jacket, three load cells with summing block/display, BPC pressure monitor, probe support system, and standard tool set.

Part Number	Description
SV50223.11	2000 L S.U.B. Water Jacket, Modbus Plus Interface (240 VAC)
SV50223.12	2000 L S.U.B. Water Jacket, Allen-Bradley Interface (240 VAC)
SV50223.13	2000 L S.U.B. Water Jacket, Analog Output Interface (240 VAC)
SV50223.14	2000 L S.U.B. Water Jacket, Profibus Interface (240 VAC)
SV50223.15	2000 L S.U.B. Water Jacket, DeviceNet Interface (240 VAC)

The S.U.B. Condenser System consists of a cart and brackets, a condenser (chill) plate, a peristaltic pump, and a chiller (temperature control unit or TCU).

Part Number	Description
SV50232.01	Complete Condenser System (120 V) including cart, chill plate and mounting post with filter brackets, chiller, and pump
SV50232.02	Complete Condenser System (240 V) including cart, chill plate and mounting post with filter brackets, chiller, and pump
SV50232.21	Condenser assembly including chill plate and mounting post with filter brackets (Option: Allowing two chill plates per system)
SV50232.23	Thermoflex 900 TCU (115 VAC/60 Hz) with necessary plumbing
SV50232.24	Thermoflex 900 TCU (240 VAC/50 or 60 Hz) with necessary plumbing
SV50241.01	Thermo Scientific Masterflex Peristaltic Pump with dual head (115 VAC/50 or 60 Hz or 230 VAC/50 or 60 Hz)

5.3 Ordering Information

Accessories

Part Number	Description
SH30720.01	Bioreactor Probe Assembly (non-sterile)
SH30845.01	Sterile Sampling Manifold with luer lock (individual)
SH30845.02	Sterile Sampling Manifold with luer lock (10 count)
SV20664.01	Heavy Duty Tubing Clamp
SV20664.02	Heavy Duty Tubing Clamps (4 pack of SV20664.01)
SV20664.03	Heavy Duty Tubing Clamps (10 pack of SV20664.01)
SV20750.01	S.U.B. Temperature/Sample Port
SV50177.01	Autoclave Tray for Probe Kits (stainless steel)
SV50177.110	16 Pin communication cable (male end one end)
SV50177.111	2 Pin heater on/off cable for external control
SV50177.16	Elevated Single Filter Bracket Assembly for 50, 100 and 250 L
SV50177.17	Elevated Filter Bracket Assembly 25.5" for dual filters–fits all sizes except 1000 L jacketed S.U.B. and 2000 L S.U.B.
SV50177.20	Elevated Dual Filter Bracket for 1000 L jacketed S.U.B.
SV50177.21	Adapter piece for 1000 L resistive heater S.U.B. to enable use of SV50177.17
SV50177.23	Probe Hanger Clip (2000 L S.U.B. only)
SV50177.65	Frit Sparge Line Support
SV50191.01	Vent Filter Heater with programmable controller (100-120 VAC)
SV50191.01-09	Vent Filter Heater and Cord Options (For use with exhaust filters when not using condenser system.)
SV50191.02	Standard filter heater power cord for US/Japan, NEMA 5-15P w/6' lead (100-120 VAC)
SV50191.03	Vent Filter Heater with programmable controller (200-240 VAC)
SV50191.04	Custom filter heater power cord for use in UK, BS1363 w/10' lead (240 VAC)
SV50191.05	Custom filter heater power cord for use in Europe, CEE 7/7 w/12' lead (240 VAC)
SV50191.06	Custom Power Cord for US/Japan, NEMA 5-15P w/ 12' leads & GFCI (100-120 VAC)
SV50191.07	Custom Power Cord for UK, BS1363 w/ 12' leads & GFCI (240 VAC)
SV50191.08	Custom Power Cord for Europe, CEE 7/7 w/ 12' leads & GFCI (240 VAC)
SV50191.09	Custom Extension Cord for filter heater, for use between heater and controller, 10' (100-240VAC)
SV50191.10	Vent Filter Heater with RTD (two wire Pt-100), (100-120 VAC/17-24 W)
SV50191.11	NEMA rated Vent Heater w/ Controller (100-120VAC), power cord (for Pall KA3 filter)
SV50191.13	NEMA rated Vent Heater w/ Controller (200-240VAC), power cord (for Pall KA3 filter)
SV50191.16	NEMA rated Vent Heater w/ Controller (100-120VAC) (for Meissner 10" filter)
SV50191.17	NEMA rated Vent Heater w/ Controller (200-240VAC) (for Meissner 10" filter)
SV50191.18	NEMA rated Vent Heater w/ Controller (200-240VAC) (for Meissner 10" filter)
SV50191.19	NEMA rated Vent Heater w/ Controller (200-240VAC) (for Meissner 10" filter)
SV50193.10	250 L, 500 L Load Cell Kit - Analog load cells (3), display, choice of interface
SV50194.10	50 L, 100 L Load Cell Kit - Analog load cells (3), display, choice of interface
SV50177.258	Dual Filter Bracket for 2000 L S.U.B. tank (when not using condenser system). Accommodates two vent filter heater units.
SV50935.01	Mobile Stairs (2000 L S.U.B. only)

5.4 Ordering Information

Partial Spare Parts List

Part Number	Description
SV50177.01	Probe Kit Autoclave Tray (SST w/Plastic Carry handle)
SV50177.02	Probe Holder, retains Probe Adapters in Closed Position (SST)
SV50177.03	Filter Bracket Assembly, 11", Single Filter (Anodized Aluminum)
SV50177.06	Motor Sleeve Cap-threaded (Anodized Aluminum)
SV50177.10	2" Open End Wrench (Anodized Aluminum)
SV50177.11	Torque Wrench-3/8" Drive-150 in-lbs (Plated Steel Construction)
SV50177.12	Stretch Hooks (Rubber w/SST hooks)
SV50177.15	Filter Bracket Assembly, 18", Single Filter (Anodized Aluminum)
SV50177.16	Filter Bracket Assembly, 24", Single Filter (Anodized Aluminum)
SV50177.17	Filter Bracket Assembly, 25.5", Dual Filter (Anodized Aluminum & SST)
SV50177.18	Filter Bracket, Dual Filter (SST) 1000 L Jacketed S.U.B.
SV50177.19	Filter Bracket, Dual Filter (SST), 1000 L Resistive S.U.B.
SV50177.20	Filter Bracket Assy, Dual Filter (SST), 1000L Jacketed S.U.B.
SV50177.34	Drive Shaft Assembly, 50 L S.U.B. (One (1) Piece Integrated Design) (Delrin/ Anodized Aluminum)
SV50177.35	Drive Shaft Assembly, 250 L S.U.B. (One (1) Piece Integrated Design) (Delrin/ Anodized Aluminum)
SV50177.36	Drive Shaft Assembly, 500 L S.U.B. (Two (2) Piece Integrated Design) (Delrin/ SST)
SV50177.38	Drive Shaft Assembly, 1000 L S.U.B. (Three (3) Piece Integrated Design) (Delrin/ SST)
SV50177.39	Drive Shaft Assembly, 1000 L S.U.B. (Four (4) Piece Integrated Design) (Delrin/ SST) (NON- Released Engineering Design)
SV50177.40	Drive Shaft Assembly, 250 L S.U.B. (One (1) Piece Integrated Design) (Delrin/ SST)
SV50177.41	Drive Shaft Assembly, 250 L S.U.B. (Two (2) Piece Integrated Design) (Delrin/ SST)
SV50177.65	Frit Sparge Line Support
SV50177.90	Safety Cap, Drive Shaft/Motor Assembly (Clear Lexan)
SV50177.110	Cable Assembly, 16 Pin, Main communication cable from S.U.B./S.U.M. to External Controller (Male one end)
SV50177.112	Cable Assembly, 16 Pin, Main communication cable from S.U.B./S.U.M. to External Controller (Male-2-Male)
SV50177.113	Cable Assembly, 16 Pin, Main communication cable from S.U.B./S.U.M. to External Controller (Male one end) (VFD & Temperature control only)
SV50177.114	Cable Assembly, 3 Pin, Pressure Alarm Relay cable from S.U.B./S.U.M. to External Controller (Male-2-Male)
SV50177.117	Cable Assembly, 4 Pin, TCU Communicaiton cable (Male one end)
SV50177.118	Cable Assembly, 4 Pin, Disposable pressure sensor communication cable w/Buccaneer QC Male & Female components.
SV50177.119	Cable Assembly, 16 Pin w/3 Pin RTD in-line QC pigtail, Main communication cable from S.U.B./S.U.M. to External Controller (Male one end & 3 Pin QC pigtail)
SV50177.124	1/4" Dia Neoprene Rubber Cord

Partial Spare Parts List (Cont.)

Part Number	Description
SV50177.155	Drive Shaft Assembly, 2000 L S.U.B. (Four (4) Piece Integrated Design)
SV50177.160	Motor, 1/4HP, 208VAC, 3Ph, IP65,10:1 Gear Reduction, 50 L, 100 L S.U.B.s
SV50177.161	Motor, 1/4HP, 208VAC, 3Ph, IP65, 12.5:1 Gear Reduction, 250 L S.U.B.
SV50177.162	Motor, 1/2HP, 208VAC, 3Ph, IP65, 15:1 Gear Reduction, 500 L, 1000 L S.U.B.s
SV50177.165	PressureMAT, Control Monitor, 1 Relay/1 Analog, 12-24VDC, 4 Watt
SV50177.166	PressureMAT, Control Monitor, 2 Relay/2 Analog (or 4 relays), 12-24VDC, 4 Watt
SV50177.170	Load Cell, 250 lbs (110 Kg), Set of 3 w/ Summing Block
SV50177.171	Load Cell, 500 lbs (220 Kg), Set of 3 w/ Summing Block
SV50177.172	Load Cell, 2150 lbs (550 Kg), Set of 3 w/ Summing Block
SV50177.173	Load Cell, 2500 lbs (1100 Kg), Set of 3 w/ Summing Block
SV50177.174	Load Cell, 5000 lbs (2200 Kg), Set of 3 w/ Summing Block
SV50177.187	Illuminated Switch, Green, 120VAC
SV50177.188	Illuminated Switch, Green, 240VAC
SV50177.189	Illuminated Light, Green, 6VDC
SV50177.193	Lamp, Green, 120VAC, Replacement for motor on/off switch
SV50177.194	Lamp, Green, 240VAC, Replacement for motor on/off switch
SV50177.208	Fuse, 10 Amp, 250VAC
SV50177.209	Fuse, 15 Amp, 250VAC
SV50177.222	Illuminated Knob, Green, Replacement for motor on/off switch
SV50177.232	RTD, PT100, 3 Wire, 60" w/o Quick Disconnect Connector (Refer to P/N TX-10289)
SV50177.233	RTD, PT100, 3 Wire, 120" w/o Quick Disconnect Connector (Refer to P/N TX-10324)
SV50177.234	RTD-Standard, PT100, 3 Wire, 60" With Quick Disconnect (Bulgin 3-pin) Connector (Refer to P/N TX-10289)
SV50177.235	Cable Assy, Disposable Sensor Fiber Optic, (DO Sensor, Green Body), Mates to SV20963 sensors
SV50177.236	Cable Assy, Disposable Sensor Fiber Optic, (PH Sensor, Blue Body), Mates to SV20963 sensors
SV50177.238	Pressure Transducer, Disposable, 12" length, QC w/4-Wire pigtail

5.5 Ordering Instructions

Disposable and hardware components for the Single-Use Bioreactor (S.U.B.) can be ordered directly from your sales representative for Thermo Scientific HyClone products. These items include all components that have part numbers beginning with the following two digits:

- SH
- SV

5.6 Ordering/Support Contact Information

In the Americas and Asia:	**In Europe:**
Tel: +1 (435) 792 8000	Tel: +32 53 85 75 59
Toll-free: +1 (800) HyClone	Fax: +32 53 85 74 31
Or +1 (800) 492 5663	perbio.euromarketing@thermofisher.com
Fax: +1 (435) 792 8001	www.thermo.com/perbio
www.thermoscientific.com/hyclone	
Info@hyclone.com	

Technical Support

Technical support for the Single-Use Bioreactor is available through a variety of formats. Some or all of the following may be appropriate depending on individual experience and circumstances.

Technical Service Hotline

Contact your Thermo Scientific HyClone sales representative for general product pricing, availability, delivery, order information and product complaints.

Call 1-800-HyClone (US) or 32 53 85 75 59 (EU) for direct and immediate response to overall product questions, and general product technical information (Technical Support). You can also contact our Tech Support by email at: hyc.bpctechsupport@thermofisher.com.

Initial Setup and Operation

Appropriate technical support is available to assist in the initial setup and operation of each Single-Use Bioreactor system. Inquire at the time of purchase.

Training

Training can be provided for startup and operation of the S.U.B. Contact your Thermo Scientific HyClone Products sales representative.

Appendix A Installation of Female Electrical Receptacle

1. In order complete this installation the facility must be equipped with an electrical housing of sufficient size.
    - Typically in the U.S. the plug will require a 'two gang box' when using the adapter plate (supplied).
    - For installations outside the U.S. (an adapter plate is not supplied) it is recommended that an electrical panel be modified to accommodate the cutout dimensions as shown below.

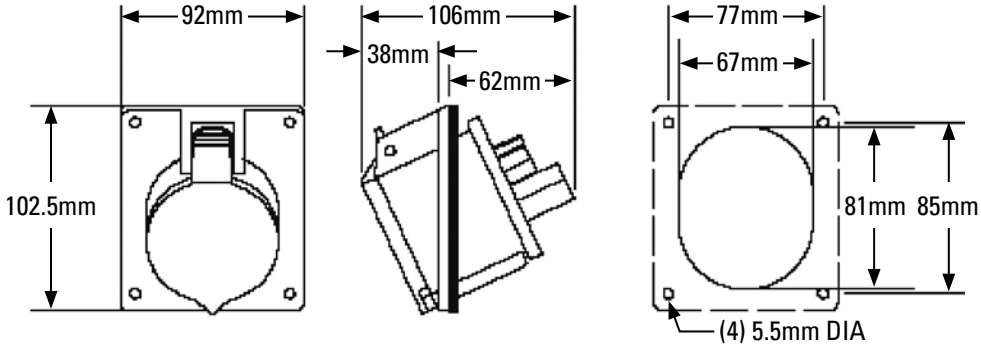

Figure 1 Panel Cutout

2. Verify that electrical power has been disconnect and been locked out for safety
3. Verify the holes for mounting the receptacle housing are positioned properly.
    - Center to center of respective mounting positions is 3.35" (85mm) tall and 3.0" (77mm) wide.
4. Verify the condition of the three expose wire leads, strip back to new wire if needed.
5. Connect the wire leads using the screw terminals, paying strict attention to obtain the correct wiring position as it is labeled on the receptacle.

- Green (ground)
- White (common)
- Black in the US, Blue in the EU (hot)

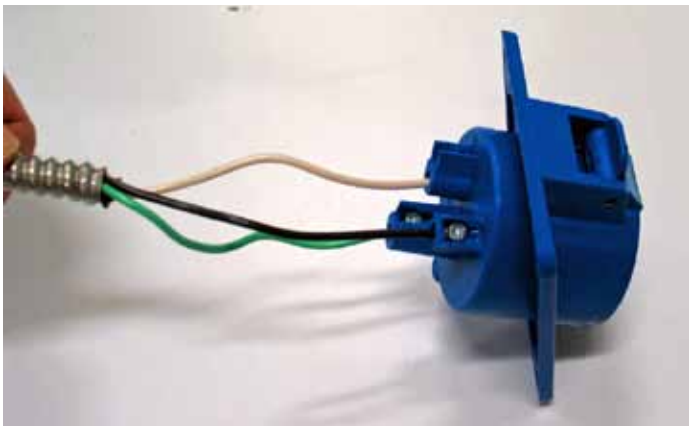

Figure 2 Female Receptacle

6. If using the adapter mounting plate, secure it to the selected facility electrical housing as per drawing (Figure 3), otherwise proceed to step 7.

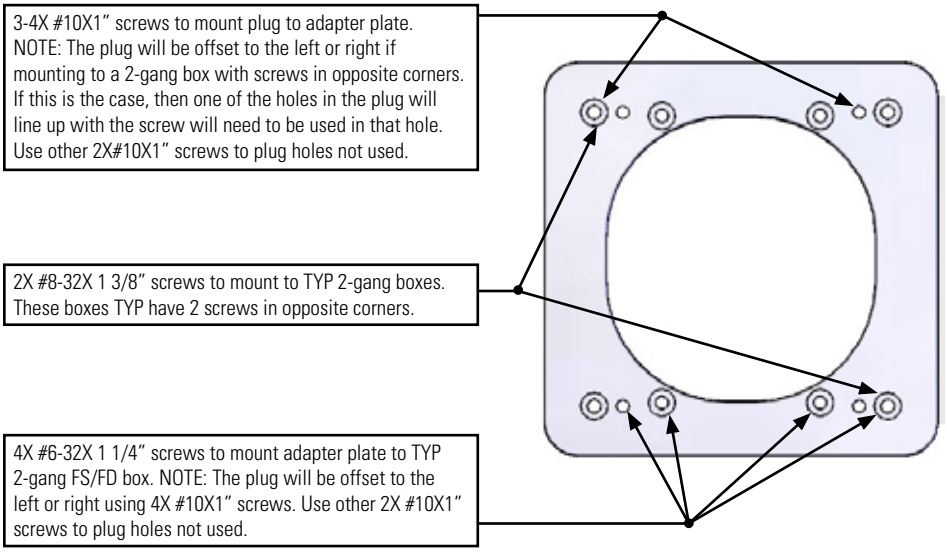

Figure 3 Adapter Mounting Plate

7. Secure the electrical receptacle using four supplied screw fasteners.
8. Connect power back to the electrical circuit.
9. Test the circuit with multi-meter prior to making any connections to the electrical receptacle.

Appendix B Calibration of the AC-Tech Variable Speed Drive

Calibration of the AC-Tech variable speed drive (SCF/SCM Models)

If during the verification of the mixer speed calibration it was determined the displayed speed varied from the actual speed, please follow these steps to calibrate the drive:

1. Press 'M' on the speed controller menu.
2. If '000' appear, the menu is locked. To unlock the menu, hold the up arrow key and select '225' then press the menu key.
3. Use the arrow key to select 'P39' and then press 'M'.
4. Use the arrow keys to enter the correct value listed in the Table 3.1, then press 'M'. **NOTE:** The value may need to be adjusted +/- slightly to calibrate exactly.

S.U.B. VFD Parameters for RPM Calibration +/- 1 rpm			
S.U.B. Unit	**Parameter**	**Value**	**Value derived from:**
50 L (SCF/SCM models)	P39	178	Motor rating of 1780 rpm (60 Hz) with gear reduction of 10:1 -- 1780/10 = 178
100 L (SCF/SCM models)	P39	178	Motor rating of 1780 rpm (60 Hz) with gear reduction of 10:1 -- 1780/12.5 = 178
250 L (SCF/SCM models)	P39	142	Motor rating of 1780 rpm (60 Hz) with gear reduction of 12.5:1 -- 1780/12.5 = 142
500 L (SCF/SCM models)	P39	356	Motor rating of 1780 rpm (60 Hz) with gear reduction of 5:1 -- 1780/5:1 = 356
1000 L (SCF/SCM models)	P39	119	Motor rating of 1780 rpm (60 Hz) with gear reduction of 15:1 -- 1780/15 = 119
2000 L (SCF/SCM models)	P39	119	Motor rating of 1780 rpm (60 Hz) with gear reduction of 15:1 -- 1780/15 = 119

Table 3.1. VFD Parameters

5. The mixer output should now be scaled properly for the correct RPM displayed.

NOTE: For users who currently operate the S.U.B. and have not previously verified the calibration of the system, the current calibration of the system should be verified so an approximate operating RPM for any previous bioreactor runs can be documented and compared to the newly calibrated system. Users can then verify the parameters in the above table and change them if necessary. To confirm that the parameter change provides a calibration accuracy of +/- 1 RPM, conduct a final check of the calibration (refer to Section 2.2). ▲

Appendix C Mettler Toledo Load Cell Calibration Instructions

Load Cell Calibration Instructions for S.U.B. Hardware Systems using Mettler Toledo Panther Display

NOTE: Please refer to the instructions and reference material found in the Panther Terminal Technical Manual for specific procedures and trouble shooting methods.

Prior to reading these instructions confirm the following:

- The Panther Display, Load Cell summing block, and Load Cell transducers have been specified, installed and configured properly.
- The load cells transducer do not have the transport lock out nuts in place (the load cells must be ready for use prior to calibration).

NOTE: The calibration accuracy achieved cannot exceed the precision of the reference used for calibration.

- Field calibration is most often performed using calibrated reference weights or flow meter for volumetric mass reference.
- Factory trained technicians have the experience and tools necessary to provide the best system performance and reliability.
- IF IN DOUBT, CONTACT THE FACTORY SERVICE REPRESENTATIVE.

Introduction

- Setup mode is accessed by pressing the “select” and “print” keys at the same time (these are the two outermost keys). See section 3 of the technical manual for further detail.
- Pressing “print” is equivalent to ENTER. Use this key to proceed through the sub-block numbers until you find the choice of interest.
- Press “select” to toggle the values of the selected sub-block
- The S.U.B. electrical schematic contains a table showing the sub-blocks that have changed from the default settings.

Calibration

(Refer to technical manual section beginning on page 3-8):

1. Access the setup menu by pressing “select” and “print” simultaneously
2. Press “print” continually until sub-block 1.4 is displayed
3. Press “print” again until [CAL X] is displayed (this is the calibration mode)
4. Press “select” to toggle the value from “0” to “1” (this will enable the calibration mode)
5. Display will show “[E SCAL]” (indicating you should now empty the scale)
6. Once the scale is empty, press “enter” (this will establish the scale zero)
7. Display will show [15 CAL] and begin to count down to zero
8. If the scale is not completely steady it may fault showing [E SCALE]
9. If successful, the display will show [Add Ld]
10. Place test (calibration) weight on scale and press “ENTER”
11. Display will show [00000]. Now enter the value of test weight.
12. Once the value is entered, press “enter” (this will establish the scale span)
13. Display will show [15 CAL] and begin to count down to zero
14. Display will show [CAL d] meaning calibration is done
15. Exit setup mode if task is complete by pressing “CLEAR”
16. Display will show [CaL.OFF]. Then press “PRINT”
17. The Panther Display will return to normal operating mode

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